```
ATG GTA CGT AGC TCC TCT CGC ACT CCG TCC GAT AAG CCG GTT GCT
M   V   R   S   S   S   R   T   P   S   D   K   P   V   A

CAT GTA GTT GCT AAC CCT CAG GCA GAA GGT CAG CTG CAG TGG CTG
H   V   V   A   N   P   Q   A   E   G   Q   L   Q   W   L

AAC CGT CGC GCT AAC GCC CTG CTG GCA AAC GGC GTT GAG CTC CGT
N   R   R   A   N   A   L   L   A   N   G   V   E   L   R

GAT AAC CAG CTC GTG GTA CCT TCT GAA GGT CTG TAC CTG ATC TAT
D   N   Q   L   V   V   P   S   E   G   L   Y   L   I   Y

TCT CAA GTA CTG TTC AAG GGT CAG GGC TGC CCG TCG ACT CAT GTT
S   Q   V   L   F   K   G   Q   G   C   P   S   T   H   V

CTG CTG ACT CAC ACC ATC AGC CGT ATT GCT GTA TCT TAC CAG ACC
L   L   T   H   T   I   S   R   I   A   V   S   Y   Q   T

AAA GTT AAC CTG CTG AGC GCT ATC AAG TCT CCG TGC CAG CGT GAA
K   V   N   L   L   S   A   I   K   S   P   C   Q   R   E

ACT CCC GAG GGT GCA GAA GCG AAA CCA TGG TAT GAA CCG ATC TAC
T   P   E   G   A   E   A   K   P   W   Y   E   P   I   Y

CTG GGT GGC GTA TTT CAA CTG GAG AAA GGT GAC CGT CTG TCC GCA
L   G   G   V   F   Q   L   E   K   G   D   R   L   S   A

GAA ATC AAC CGT CCT GAC TAT CTA GAT TTC GCT GAA TCT GGC CAG
E   I   N   R   P   D   Y   L   D   F   A   E   S   G   Q


GTG TAC TTC GGT ATT ATC GCA CTG TAA
V   Y   F   G   I   I   A   L   *
```

FIG. 1

Derivation of the VNP20009(*serC*$^{--}$) strain.

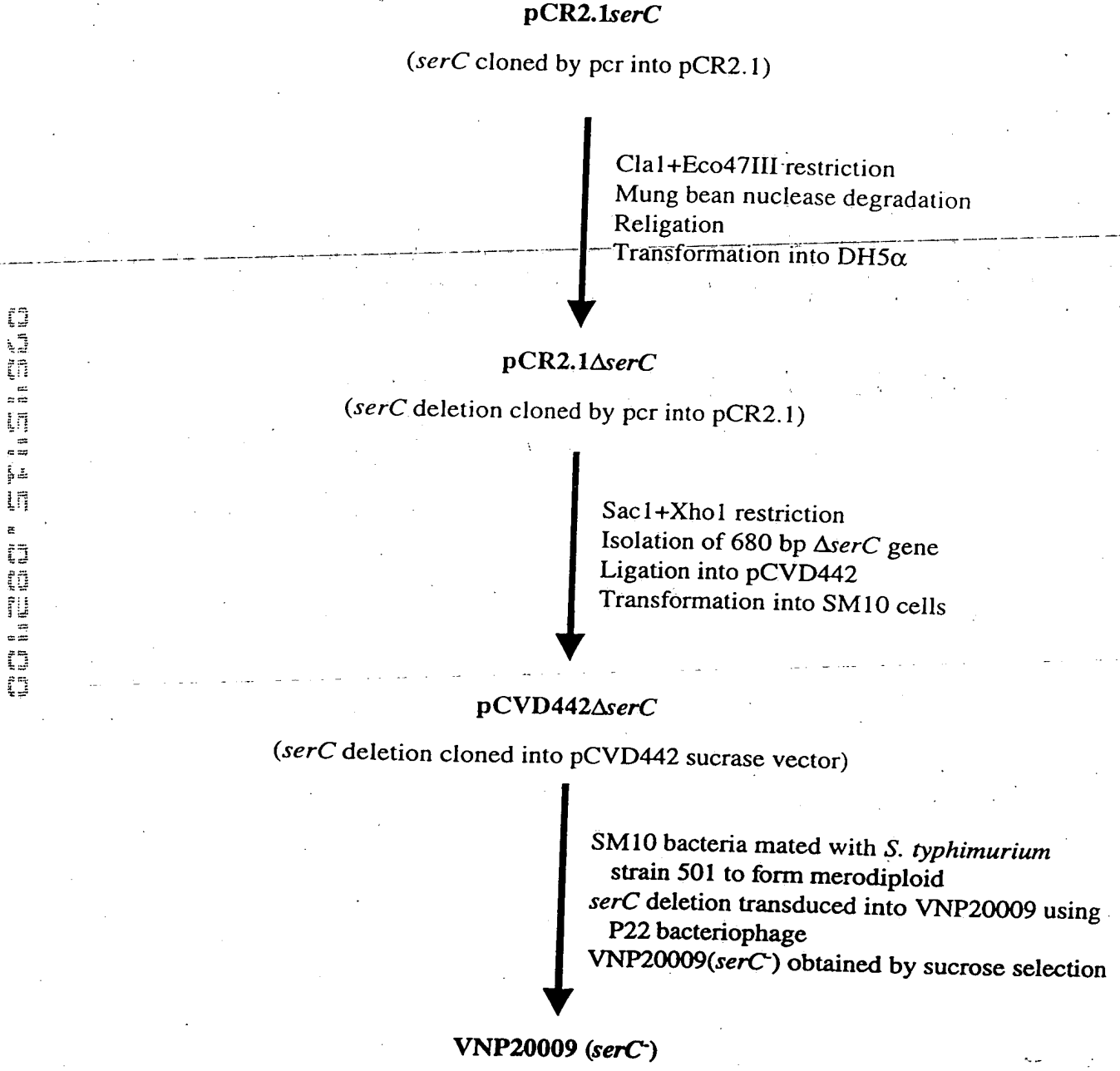


FIG. 2

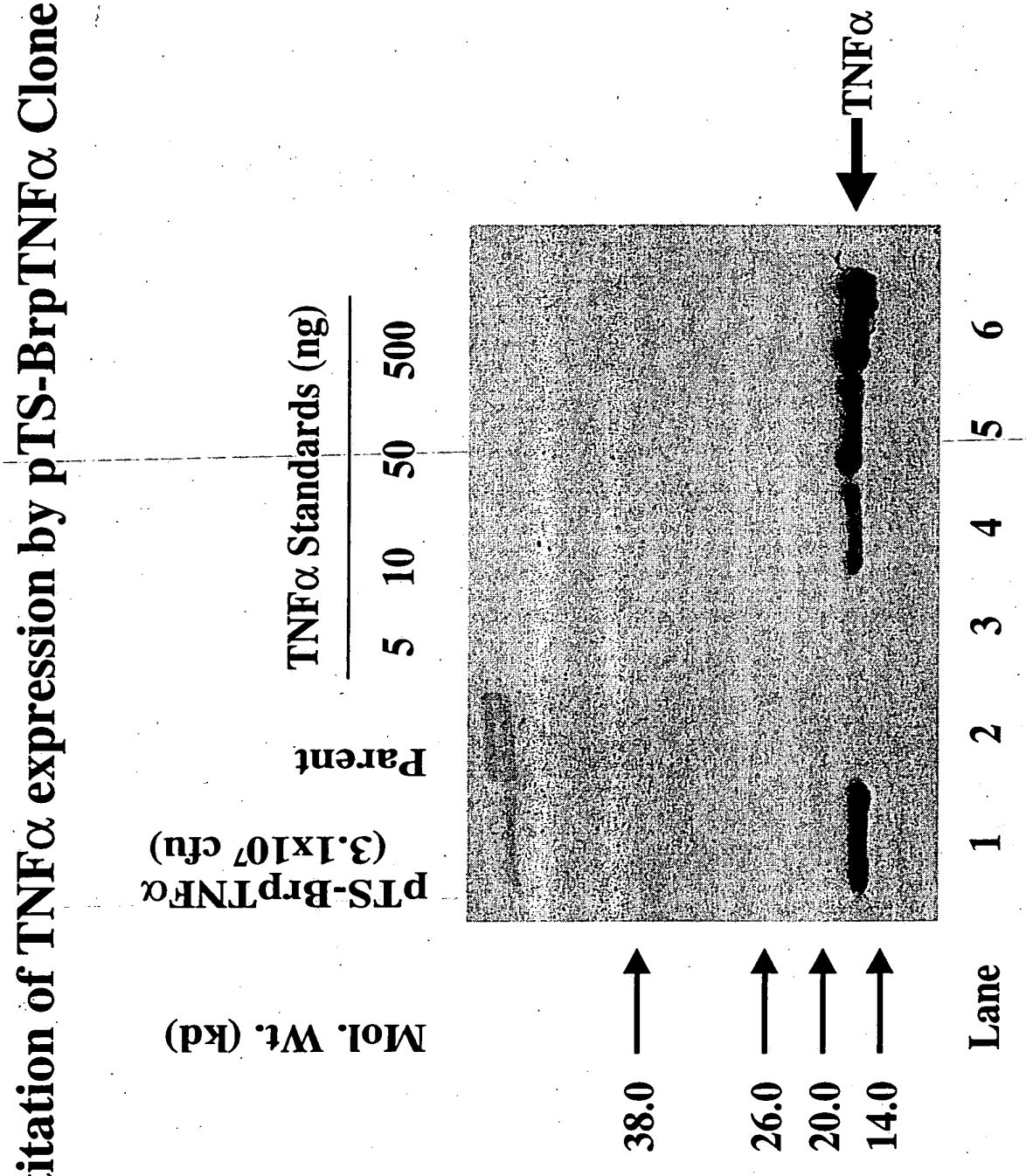

Quantitation of TNFα expression by pTS-BrpTNFα Clone 2.
TNFα
Mol. Wt. (kd)
38.0
26.0
20.0
14.0
Lane
1
2
3
4
5
6
pTS-BrpTNFα (3.1x10⁷ cfu)
Parent
TNFα Standards (ng)
5
10
50
500

FIG. 3

```
ATG AAA AAG ACA GCT ATC GCG ATT GCA GTG GCA CTG GCT GGT TTC
M   K   K   T   A   I   A   I   A   V   A   L   A   G   F

GCT ACC GTA GCG CAG GCC CAT ATG GTA CGT AGC TCC TCT CGC ACT
A   T   V   A   Q   A   H   M   V   R   S   S   S   R   T

CCG TCC GAT AAG CCG GTT GCT CAT GTA GTT GCT AAC CCT CAG GCA
P   S   D   K   P   V   A   H   V   V   A   N   P   Q   A

GAA GGT CAG CTG CAG TGG CTG AAC CGT CGC GCT AAC GCC CTG CTG
E   G   Q   L   Q   W   L   N   R   R   A   N   A   L   L

GCA AAC GGC GTT GAG CTC CGT GAT AAC CAG CTC GTG GTA CCT TCT
A   N   G   V   E   L   R   D   N   Q   L   V   V   P   S

GAA GGT CTG TAC CTG ATC TAT TCT CAA GTA CTG TTC AAG GGT CAG
E   G   L   Y   L   I   Y   S   Q   V   L   F   K   G   Q

GGC TGC CCG TCG ACT CAT GTT CTG CTG ACT CAC ACC ATC AGC CGT
G   C   P   S   T   H   V   L   L   T   H   T   I   S   R

ATT GCT GTA TCT TAC CAG ACC AAA GTT AAC CTG CTG AGC GCT ATC
I   A   V   S   Y   Q   T   K   V   N   L   L   S   A   I

AAG TCT CCG TGC CAG CGT GAA ACT CCC GAG GGT GCA GAA GCG AAA
K   S   P   C   Q   R   E   T   P   E   G   A   E   A   K

CCA TGG TAT GAA CCG ATC TAC CTG GGT GGC GTA TTT CAA CTG GAG
P   W   Y   E   P   I   Y   L   G   G   V   F   Q   L   E

AAA GGT GAC CGT CTG TCC GCA GAA ATC AAC CGT CCT GAC TAT CTA
K   G   D   R   L   S   A   E   I   N   R   P   D   Y   L

GAT TTC GCT GAA TCT GGC CAG GTG TAC TTC GGT ATT ATC GCA CTG
D   F   A   E   S   G   Q   V   Y   F   G   I   I   A   L

TAA
*
```

FIG. 4

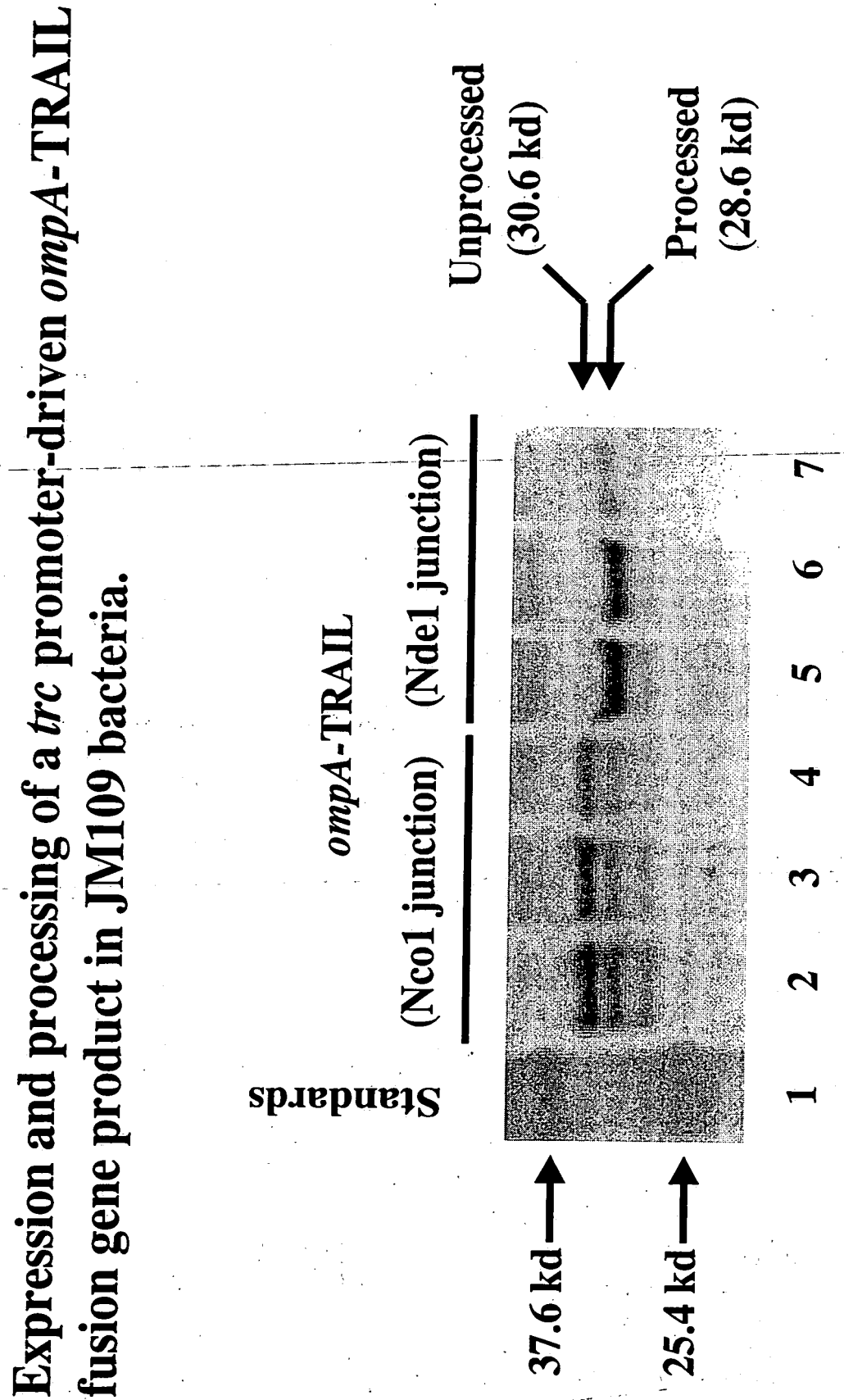

Expression and processing of a trc promoter-driven ompA-TRAIL fusion gene product in JM109 bacteria.
Unprocessed (30.6 kd)
Processed (28.6 kd)
ompA-TRAIL
(Nco1 junction) (Nde1 junction)
Standards
1 2 3 4 5 6 7
37.6 kd
25.4 kd

FIG. 5

```
ATG AAA AAG ACA GCT ATC GCG ATT GCA GTG GCA CTG GCT GGT TTC
M   K   K   T   A   I   A   I   A   V   A   L   A   G   F

GCT ACC GTA GCG CAG GCC CAT ATG GCT AAC GAG CTG AAG CAG ATG
A   T   V   A   Q   A   H   M   A   N   E   L   K   Q   M

CAG GAC AAG TAC TCC AAA AGT GGC ATT GCT TGT TTC TTA AAA GAA
Q   D   K   Y   S   K   S   G   I   A   C   F   L   K   E

GAT GAC AGT TAT TGG GAC CCC AAT GAC GAA GAG AGT ATG AAC AGC
D   D   S   Y   W   D   P   N   D   E   E   S   M   N   S

CCC TGC TGG CAA GTC AAG TGG CAA CTC CGT CAG CTC GTT AGA AAG
P   C   W   Q   V   K   W   Q   L   R   Q   L   V   R   K

ATG ATT TTG AGA ACC TCT GAG GAA ACC ATT TCT ACA GTT CAA GAA
M   I   L   R   T   S   E   E   T   I   S   T   V   Q   E

AAG CAA CAA AAT ATT TCT CCC CTA GTG AGA GAA AGA GGT CCT CAG
K   Q   Q   N   I   S   P   L   V   R   E   R   G   P   Q

AGA GTA GCA GCT CAC ATA ACT GGG ACC AGA GGA AGA AGC AAC ACA
R   V   A   A   H   I   T   G   T   R   G   R   S   N   T

TTG TCT TCT CCA AAC TCC AAG AAT GAA AAG GCT CTG GGC CGC AAA
L   S   S   P   N   S   K   N   E   K   A   L   G   R   K

ATA AAC TCC TGG GAA TCA TCA AGG AGT GGG CAT TCA TTC CTG AGC
I   N   S   W   E   S   S   R   S   G   H   S   F   L   S

AAC TTG CAC TTG AGG AAT GGT GAA CTG GTC ATC CAT GAA AAA GGG
N   L   H   L   R   N   G   E   L   V   I   H   E   K   G

TTT TAC TAC ATC TAT TCC CAA ACA TAC TTT CGA TTT CAG GAG GAA
F   Y   Y   I   Y   S   Q   T   Y   F   R   F   Q   E   E

ATA AAA GAA AAC ACA AAG AAC GAC AAA CAA ATG GTC CAA TAT ATT
I   K   E   N   T   K   N   D   K   Q   M   V   Q   Y   I

TAC AAA TAC ACA AGT TAT CCT GAC CCT ATA TTG TTG ATG AAA AGT
Y   K   Y   T   S   Y   P   D   P   I   L   L   M   K   S

GCT AGA AAT AGT TGT TGG TCT AAA GAT GCA GAA TAT GGA CTC TAT
A   R   N   S   C   W   S   K   D   A   E   Y   G   L   Y

TCC ATC TAT CAA GGG GGA ATA TTT GAG CTT AAG GAA AAT GAC AGA
S   I   Y   Q   G   G   I   F   E   L   K   E   N   D   R

ATT TTT GTT TCT GTA ACA AAT GAG CAC TTG ATA GAC ATG GAC CAT
I   F   V   S   V   T   N   E   H   L   I   D   M   D   H

GAA GCC AGT TTT TTC GGG GCC TTT TTA GTT GGC TAA
E   A   S   F   F   G   A   F   L   V   G   *
```

FIG. 6

Expression and processing of a *trc* promoter-driven *ompA*-TNFα fusion gene product in JM109 bacteria.

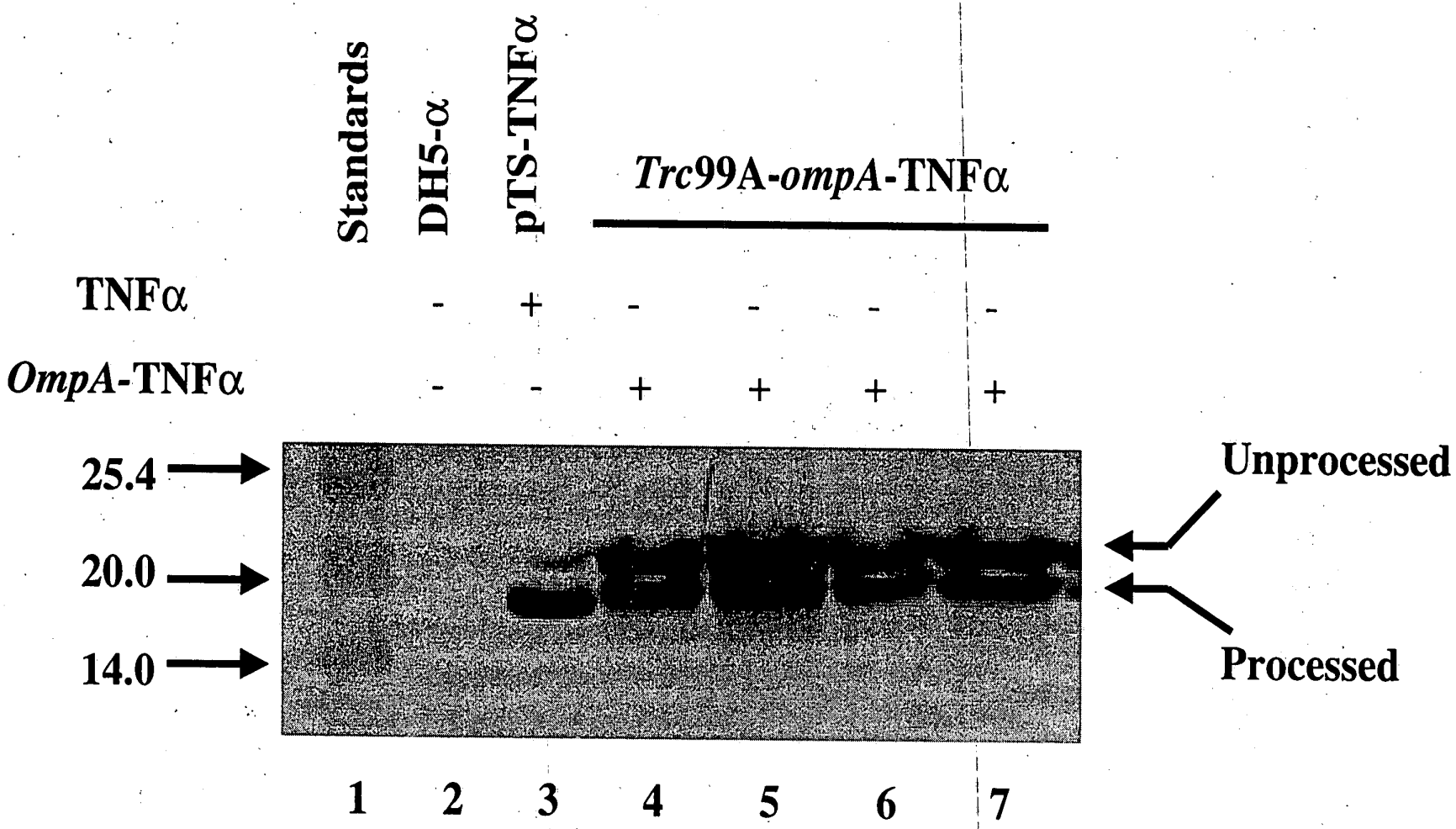


FIG. 7

```
ATG AAA AAG ACG GCT CTG GCG CTT CTG CTC TTG CTG TTA GCG CTG
M   K   K   T   A   L   A   L   L   L   L   L   A   L

ACT AGT GTA GCG CAG GCC GCT CCT ACT AGC TCG AGC ACT AAG AAA
T   S   V   A   Q   A   A   P   T   S   S   S   T   K   K

ACT CAA CTG CAA TTG GAG CAT CTG CTG CTG GAT CTG CAG ATG ATT
T   Q   L   Q   L   E   H   L   L   L   D   L   Q   M   I

CTG AAT GGC ATC AAT AAC TAC AAG AAC CCT AAG CTG ACT CGC ATG
L   N   G   I   N   N   Y   K   N   P   K   L   T   R   M

CTG ACT TTC AAA TTC TAC ATG CCG AAA AAG GCT ACC GAG CTC AAA
L   T   F   K   F   Y   M   P   K   K   A   T   E   L   K

CAT CTC CAG TGC CTG GAA GAG GAA CTG AAG CCG CTG GAG GAA GTA
H   L   Q   C   L   E   E   E   L   K   P   L   E   E   V

CTT AAC CTG GCA CAG TCT AAG AAC TTC CAC CTG CGT CCG CGT GAC
L   N   L   A   Q   S   K   N   F   H   L   R   P   R   D

CTG ATC TCC AAC ATC AAT GTA ATC GTT CTT GAG CTG AAG GGA TCC
L   I   S   N   I   N   V   I   V   L   E   L   K   G   S

GAA ACC ACC TTC ATG TGC GAA TAC GCT GAC GAA ACC GCC ACC ATT
E   T   T   F   M   C   E   Y   A   D   E   T   A   T   I

GTG GAG TTC CTG AAC CGT TGG ATC ACC TTT GCC CAA TCG ATC ATT
V   E   F   L   N   R   W   I   T   F   A   Q   S   I   I

AGC ACG TTA ACT TAA
S   T   L   T   *
```

FIG. 8

Periplasmic localization and processing of *ompA*-IL2 fusion proteins.

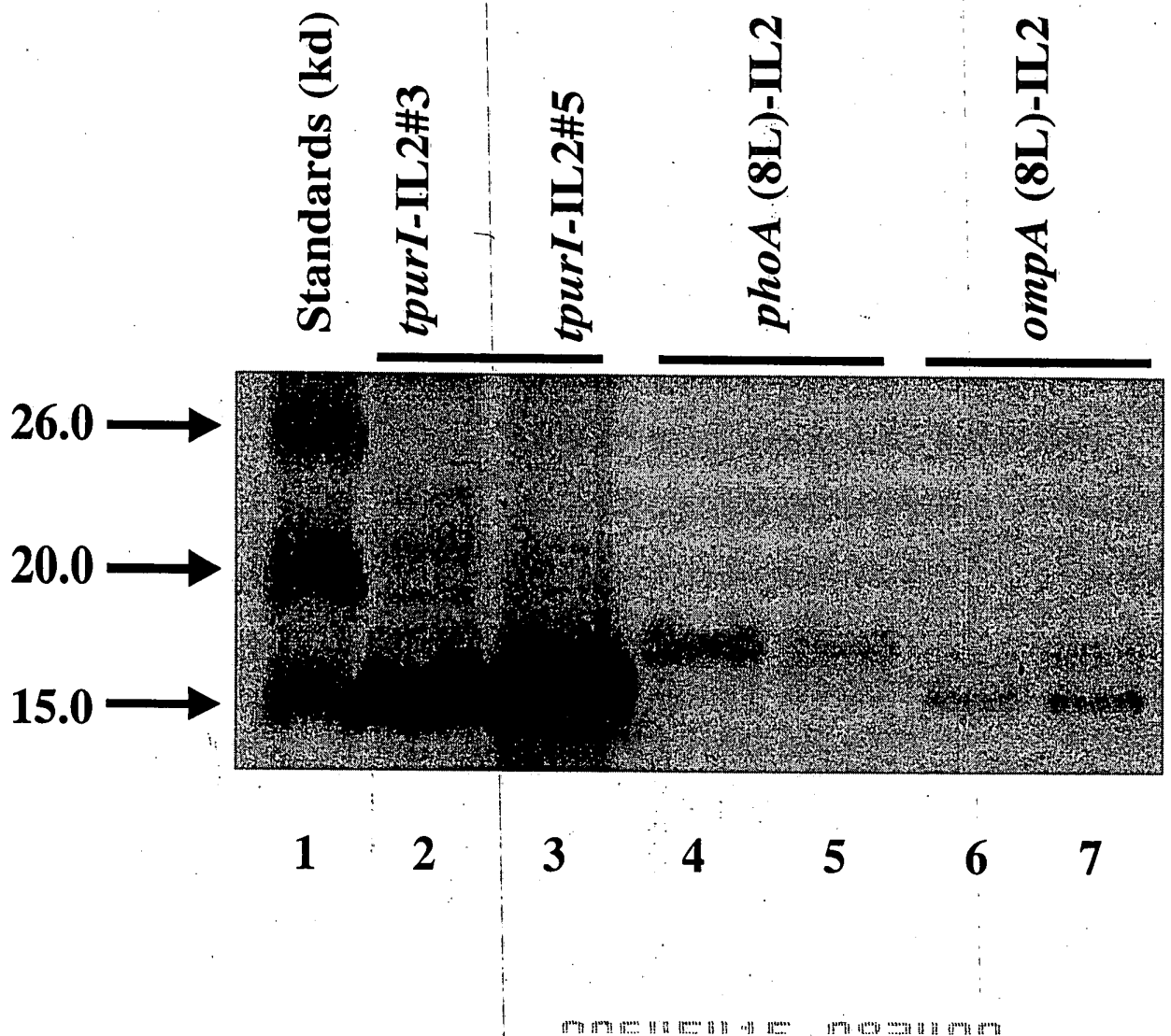


FIG. 9

MB85P131

```
ATG AAA CAG TCG ACT CTG GCG CTT CTG CTC TTG CTG TTA GCG CTG
M   K   Q   S   T   L   A   L   L   L   L   L   L   A   L

ACT AGT GTG GCC AAA GCG GCT CCT ACT AGC TCG AGC ACT AAG AAA
T   S   V   A   K   A   A   P   T   S   S   S   T   K   K

ACT CAA CTG CAA TTG GAG CAT CTG CTG CTG GAT CTG CAG ATG ATT
T   Q   L   Q   L   E   H   L   L   L   D   L   Q   M   I

CTG AAT GGC ATC AAT AAC TAC AAG AAC CCT AAG CTG ACT CGC ATG
L   N   G   I   N   N   Y   K   N   P   K   L   T   R   M

CTG ACT TTC AAA TTC TAC ATG CCG AAA AAG GCT ACC GAG CTC AAA
L   T   F   K   F   Y   M   P   K   K   A   T   E   L   K

CAT CTC CAG TGC CTG GAA GAG GAA CTG AAG CCG CTG GAG GAA GTA
H   L   Q   C   L   E   E   E   L   K   P   L   E   E   V

CTT AAC CTG GCA CAG TCT AAG AAC TTC CAC CTG CGT CCG CGT GAC
L   N   L   A   Q   S   K   N   F   H   L   R   P   R   D

CTG ATC TCC AAC ATC AAT GTA ATC GTT CTT GAG CTG AAG GGA TCC
L   I   S   N   I   N   V   I   V   L   E   L   K   G   S

GAA ACC ACC TTC ATG TGC GAA TAC GCT GAC GAA ACC GCC ACC ATT
E   T   T   F   M   C   E   Y   A   D   E   T   A   T   I

GTG GAG TTC CTG AAC CGT TGG ATC ACC TTT GCC CAA TCG ATC ATT
V   E   F   L   N   R   W   I   T   F   A   Q   S   I   I

AGC ACG TTA ACT TAA
S   T   L   T   *
```

FIG. 10

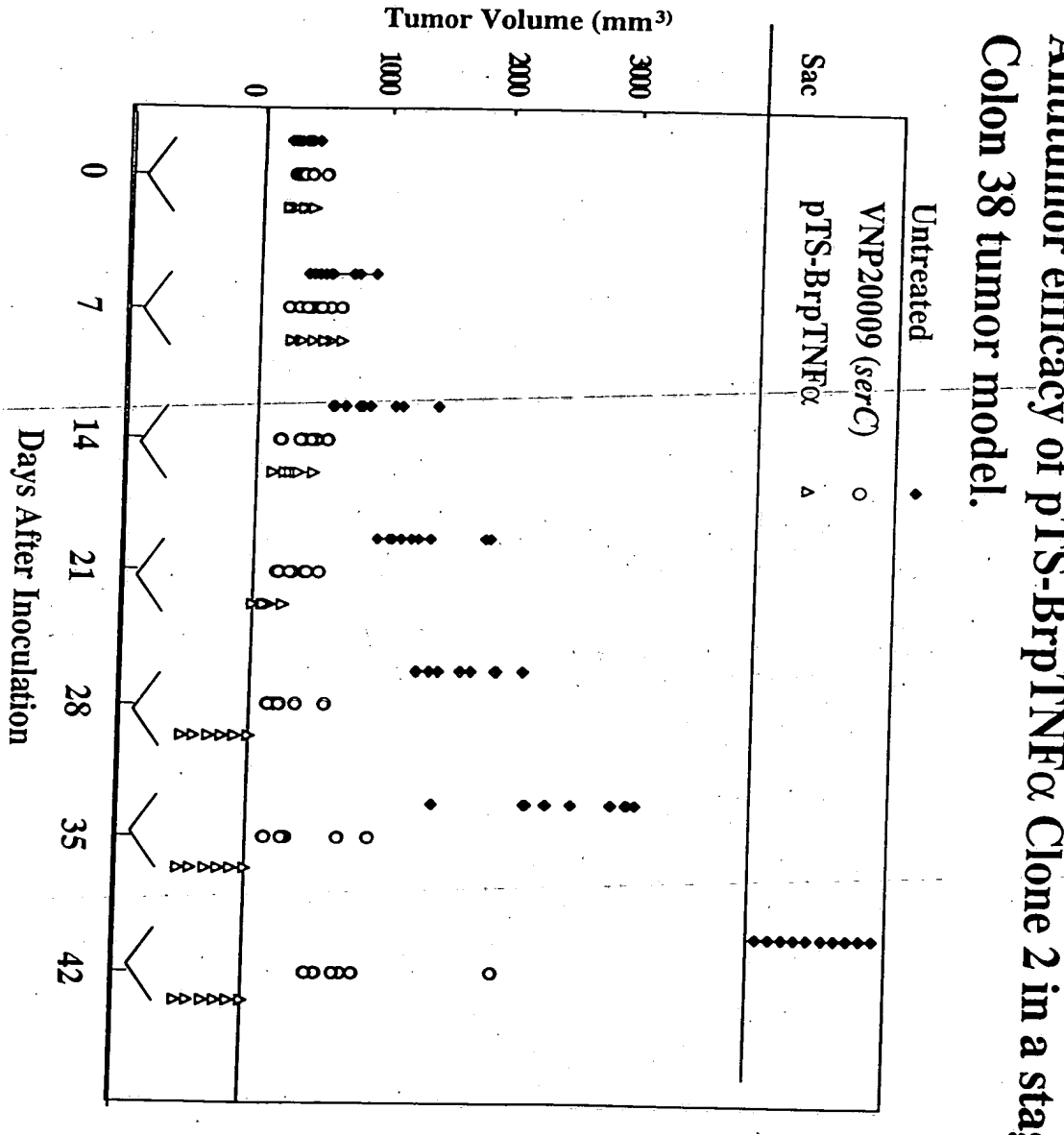

Antitumor efficacy of pTS-BrpTNFα Clone 2 in a staged Colon 38 tumor model.
Tumor Volume (mm3)
0
1000
2000
3000
Untreated
VNP20009 (serC)
pTS-BrpTNFα
Sac
0
7
14
21
28
35
42
Days After Inoculation

FIG. 11

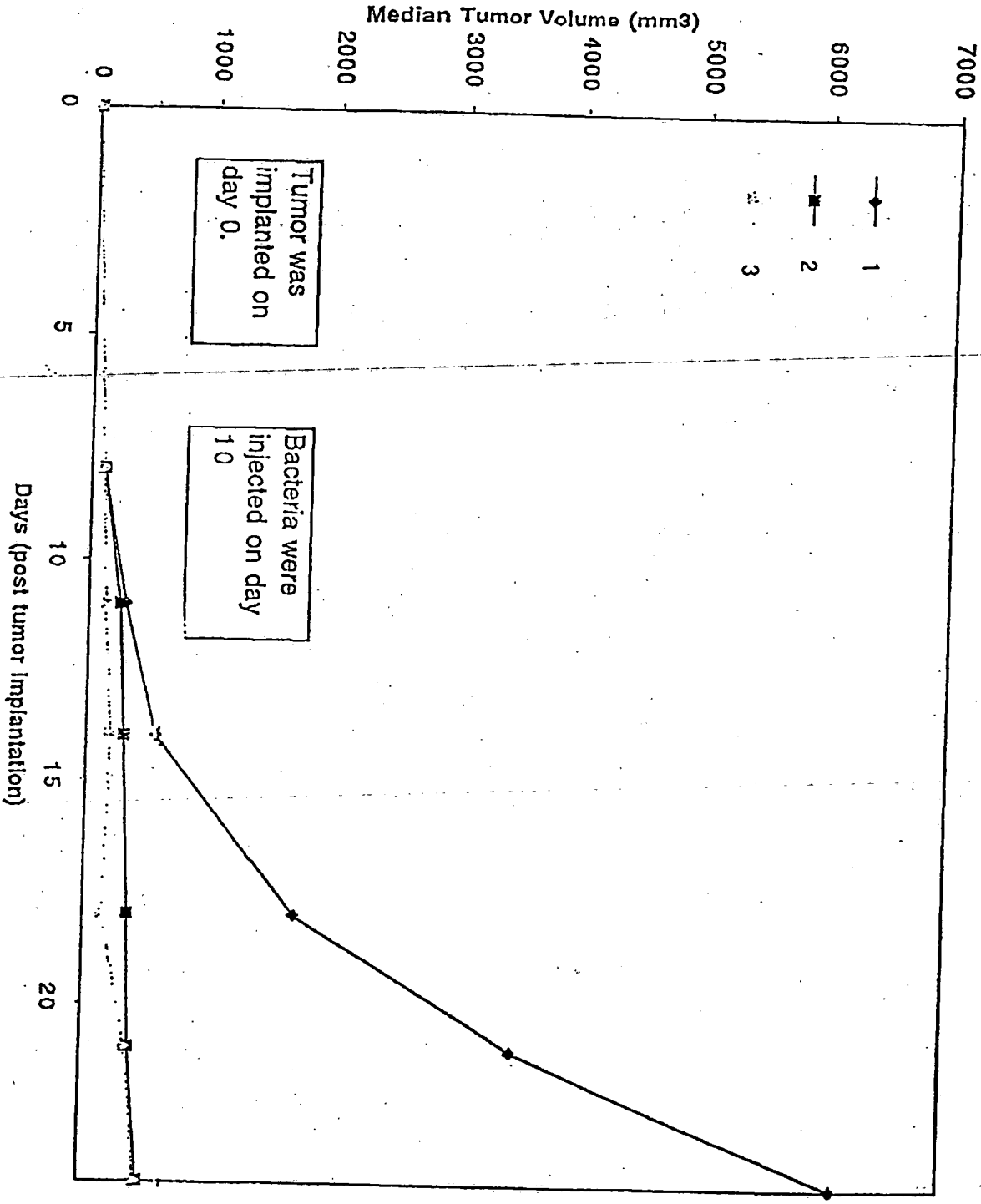

Median Tumor Volume (mm3)
0
1000
2000
3000
4000
5000
6000
7000
Days (post tumor implantation)
0
5
10
15
20
Tumor was implanted on day 0.
Bacteria were injected on day 10
1
2
3

FIG. 12

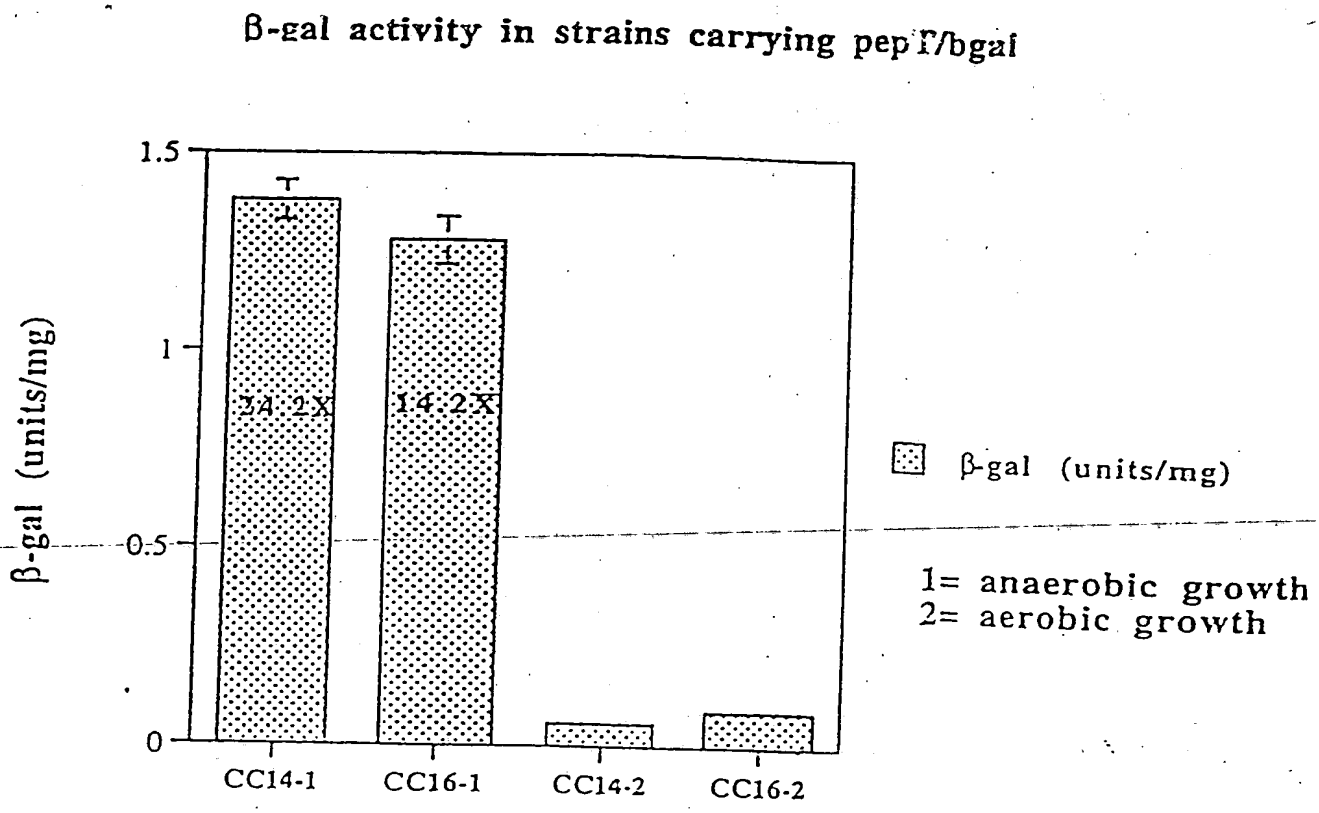


FIG. 13A

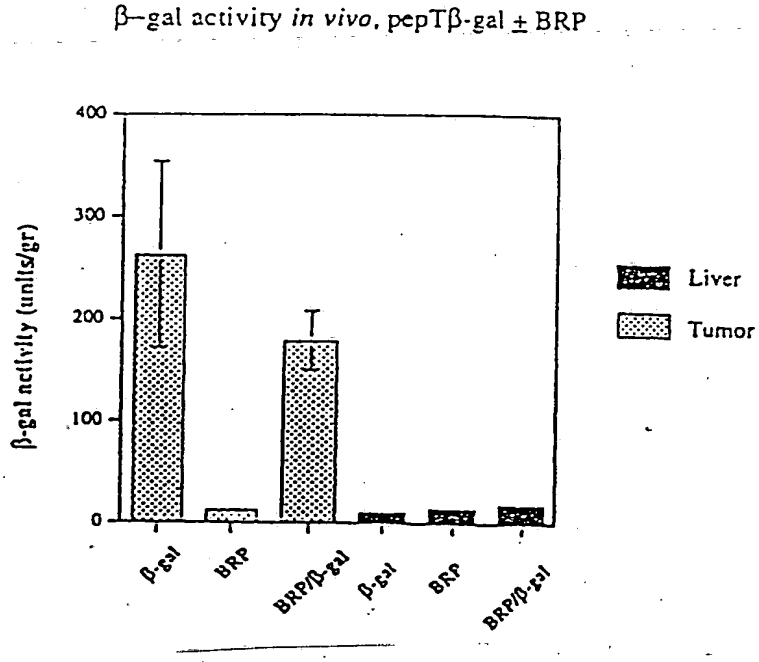


FIG. 13B

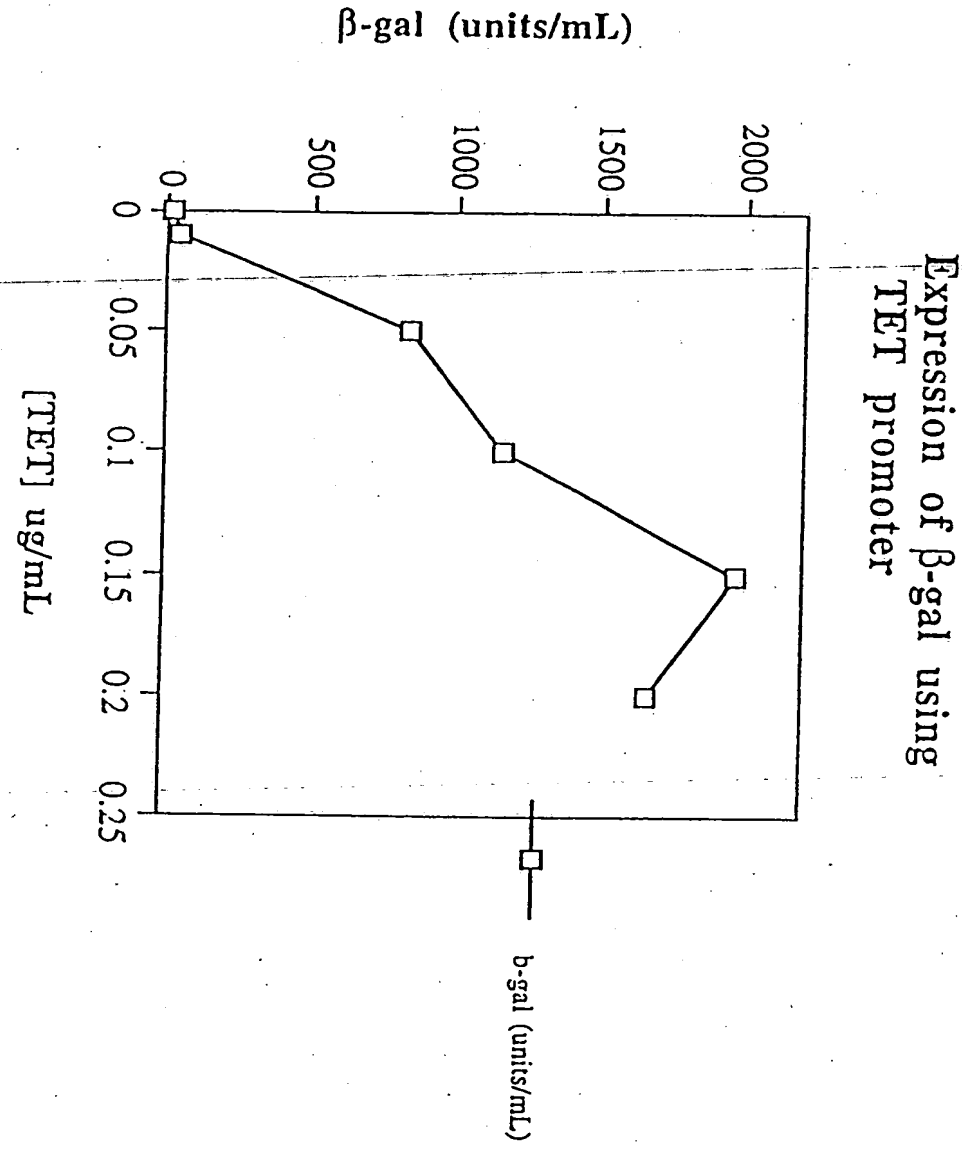
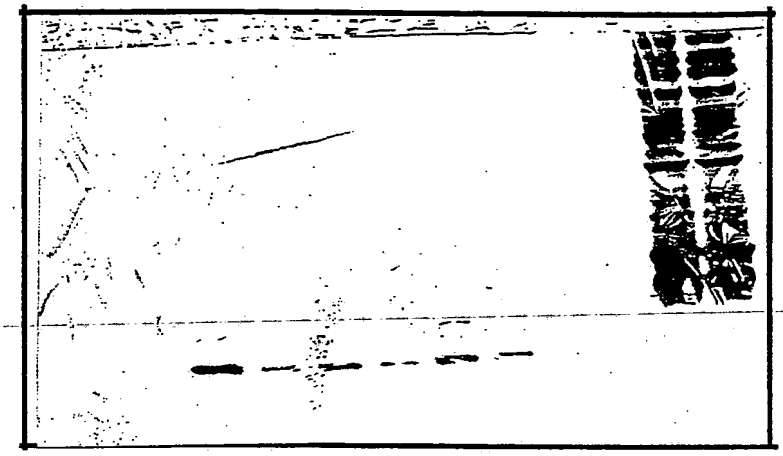

β-gal (units/mL)
0
500
1000
1500
2000
0
0.05
0.1
0.15
0.2
0.25
[TET] ug/mL
Expression of β-gal using TET promoter
b-gal (units/mL)

FIG. 14

A.



B.

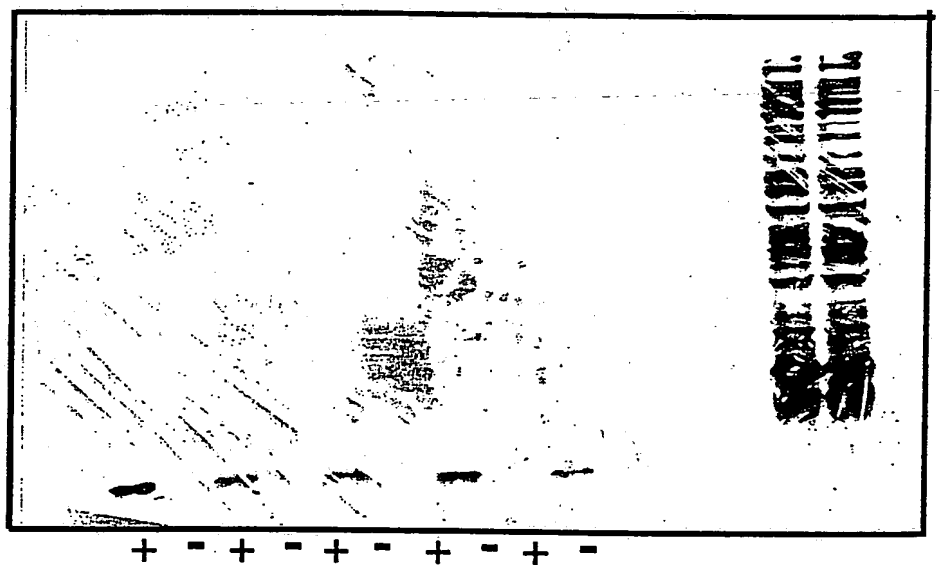


FIG. 15

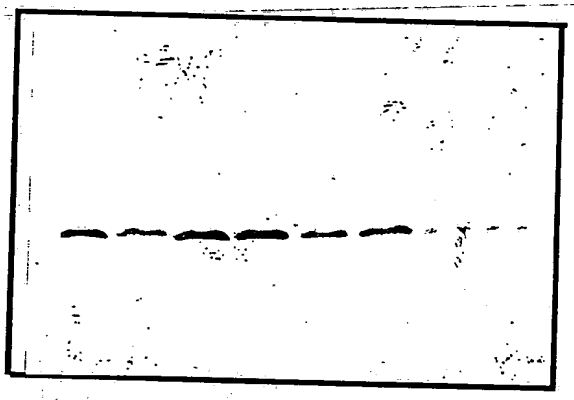


FIG. 16

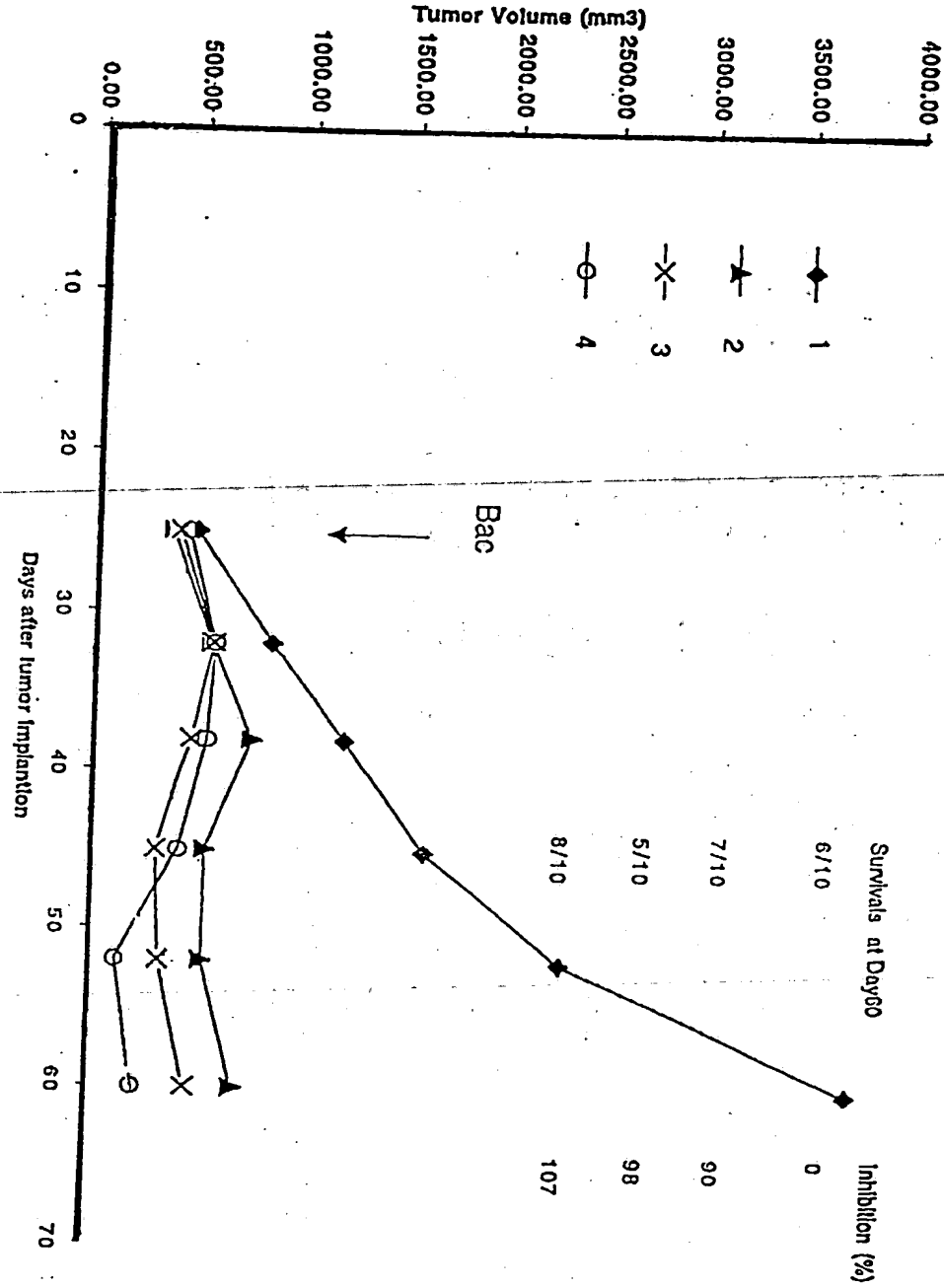

Tumor Volume (mm3)
0.00
500.00
1000.00
1500.00
2000.00
2500.00
3000.00
3500.00
4000.00
0
10
20
30
40
50
60
70
Days after tumor implantion
1
2
3
4
Bac
Survivals at Day60
6/10
7/10
5/10
8/10
Inhibition (%)
0
90
98
107

FIG. 17

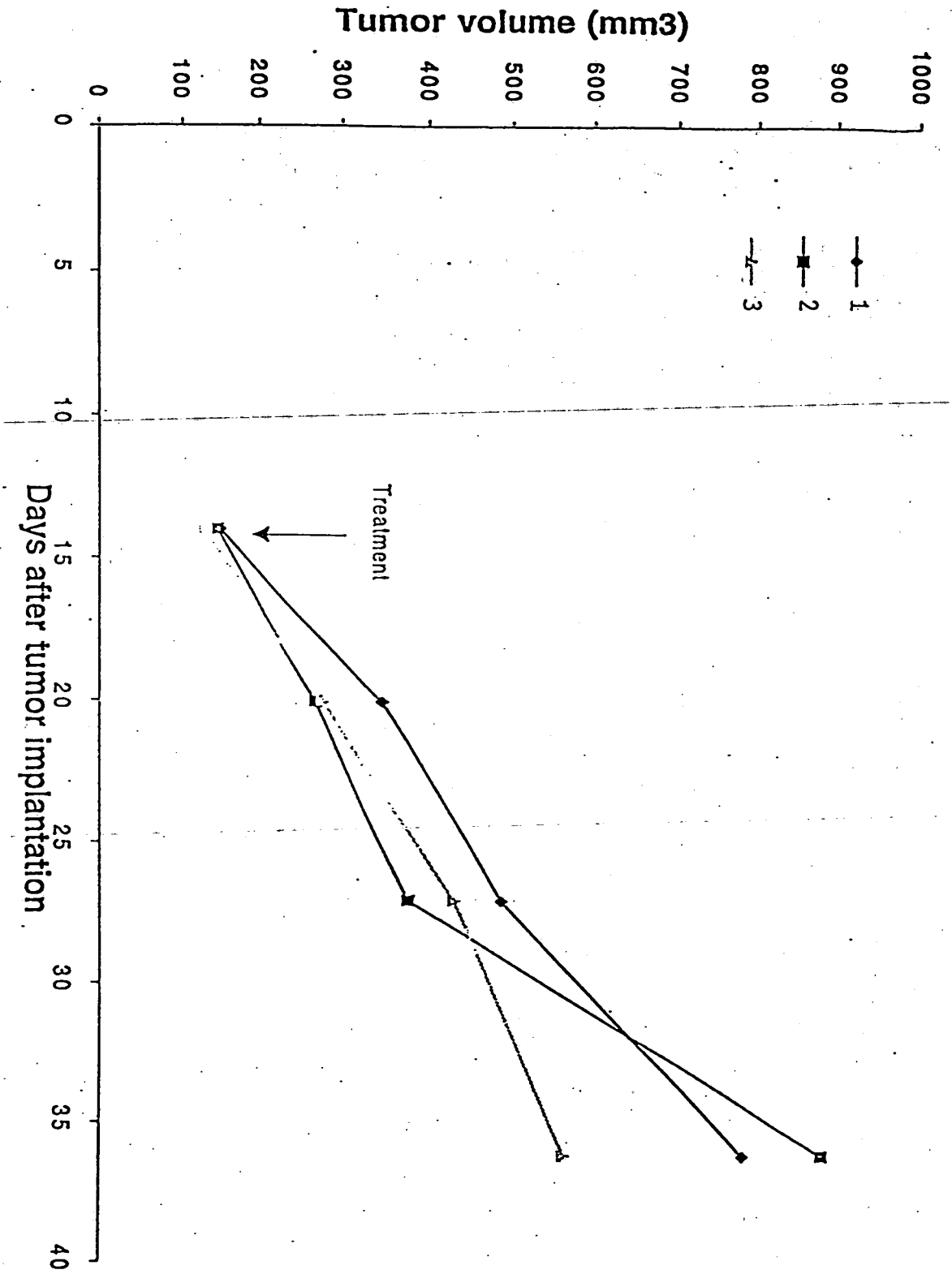

Tumor volume (mm3)
0
100
200
300
400
500
600
700
800
900
1000
0
5
10
15
20
25
30
35
40
Days after tumor implantation
Treatment
1
2
3

FIG. 18

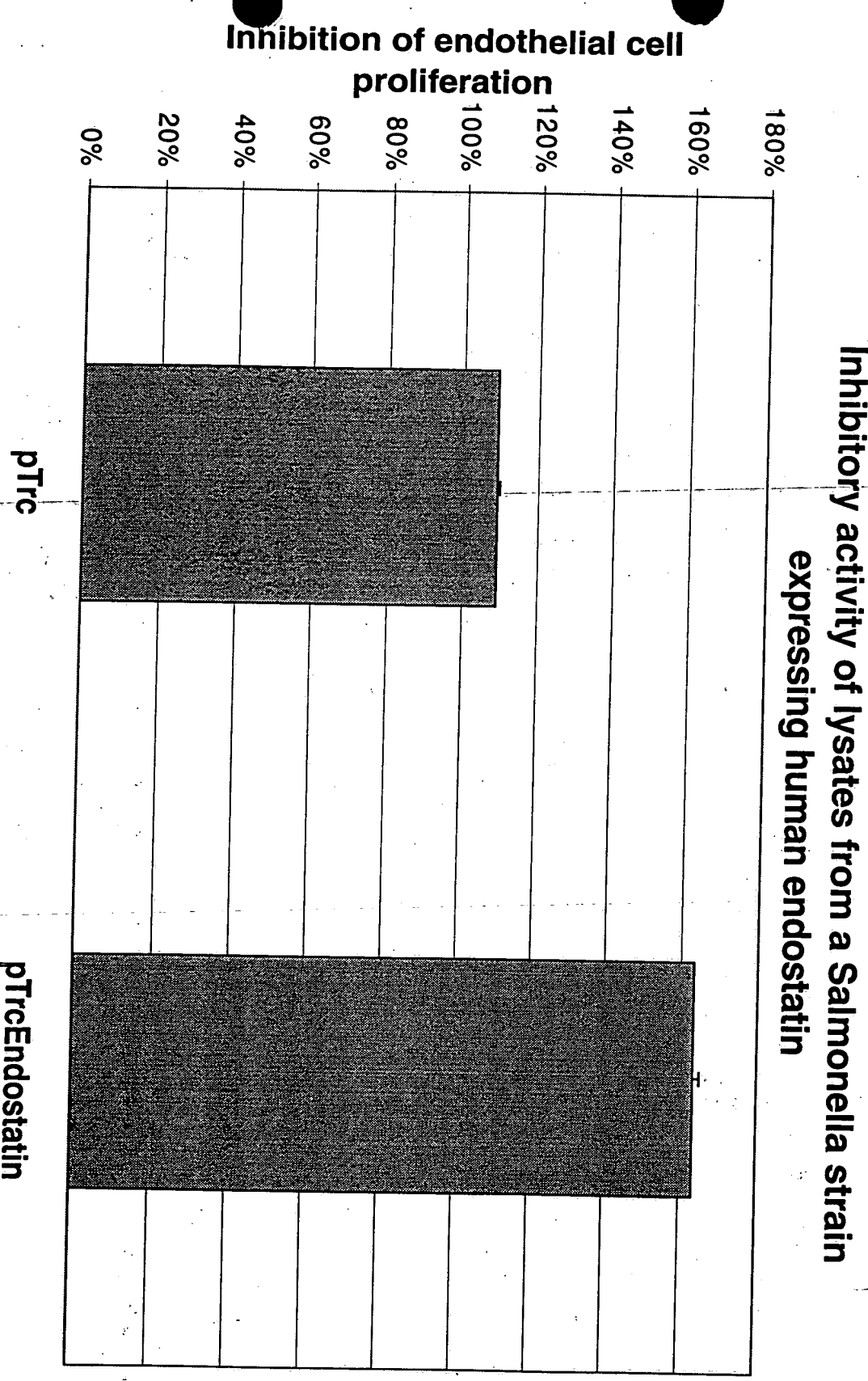

Inhibition of endothelial cell proliferation
0%
20%
40%
60%
80%
100%
120%
140%
160%
180%
Inhibitory activity of lysates from a Salmonella strain expressing human endostatin
pTrc
pTrcEndostatin

FIG. 19

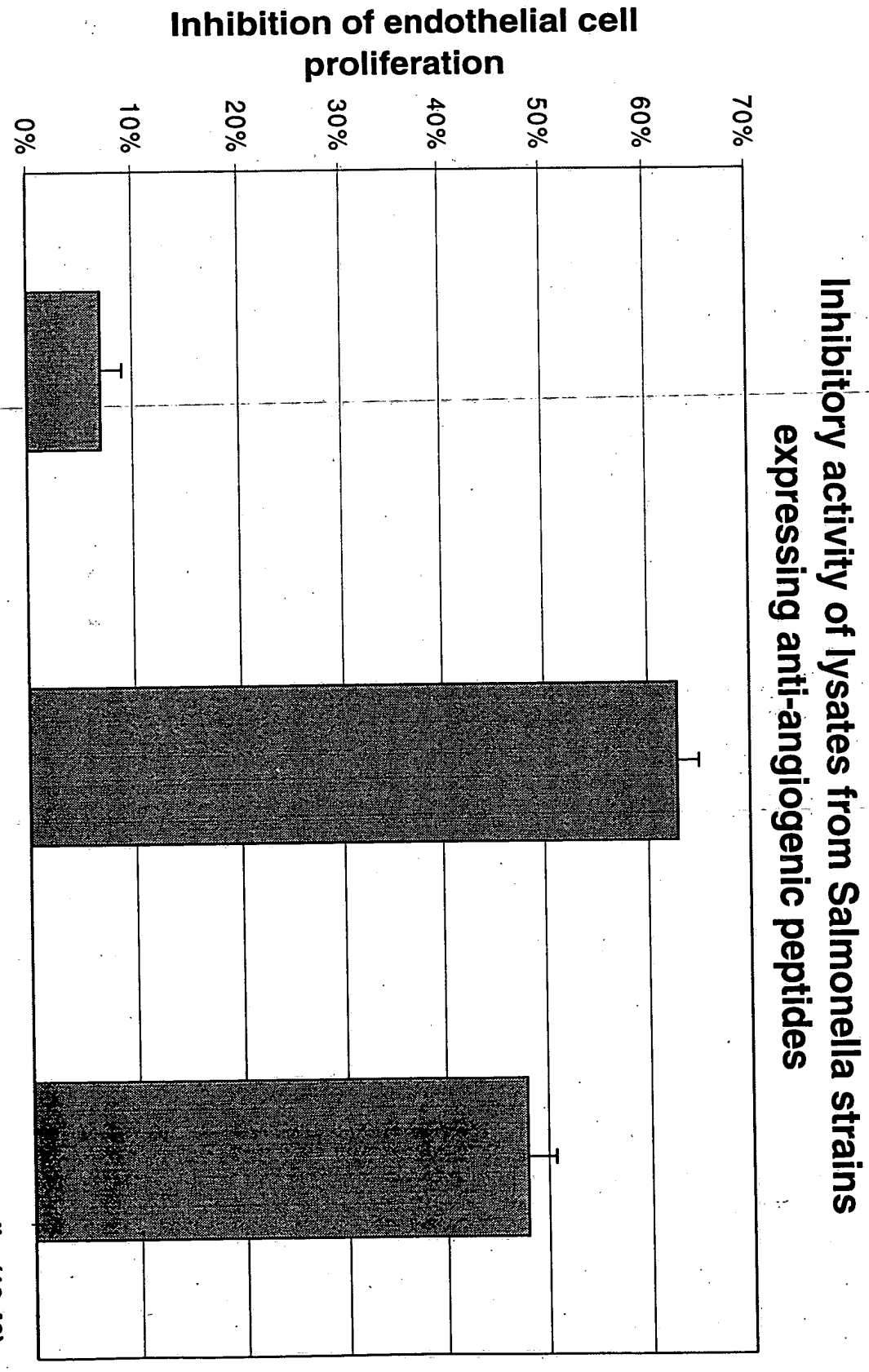

Inhibitory activity of lysates from Salmonella strains expressing anti-angiogenic peptides
Inhibition of endothelial cell proliferation
0%
10%
20%
30%
40%
50%
60%
70%
pTrc
pTrcPlatelet Factor-4 (47-70)
pTrcThrombospondin (13.40)

FIG. 20

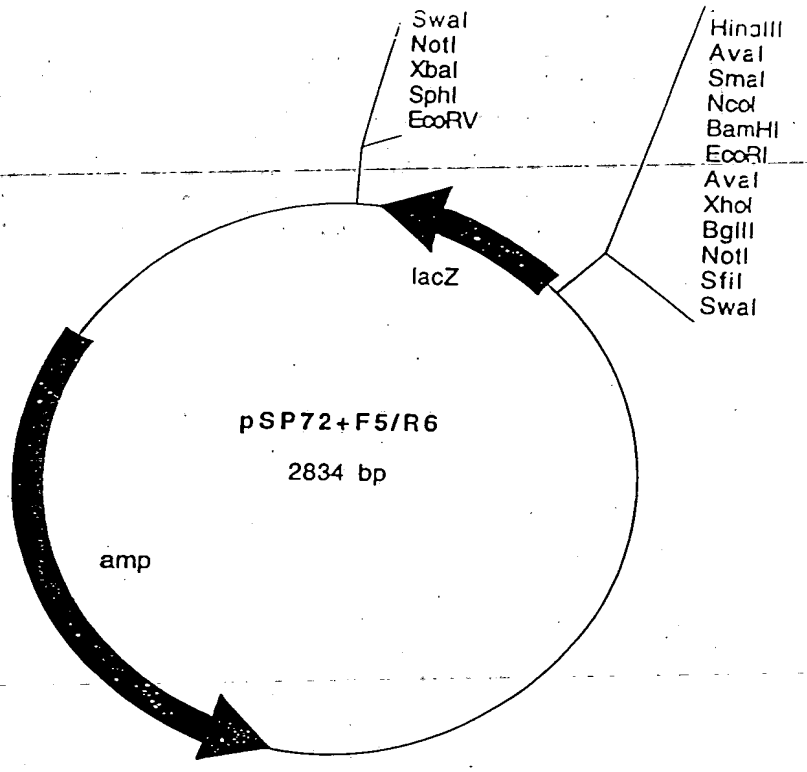

SwaI
NotI
XbaI
SphI
EcoRV
HindIII
AvaI
SmaI
NcoI
BamHI
EcoRI
AvaI
XhoI
BglII
NotI
SfiI
SwaI
lacZ
pSP72+F5/R6
2834 bp
amp

FIG. 21

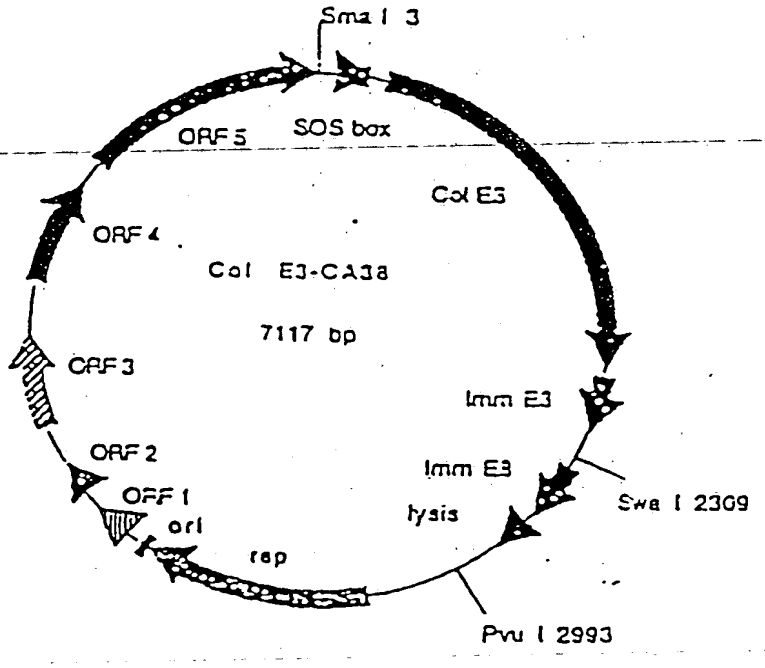

Sma I 3
ORF 5
SOS box
Col E3
ORF 4
Col E3-CA38
7117 bp
ORF 3
Imm E3
ORF 2
Imm E3
ORF 1
ori
lysis
Swa I 2309
rep
Pvu I 2993

FIG. 22

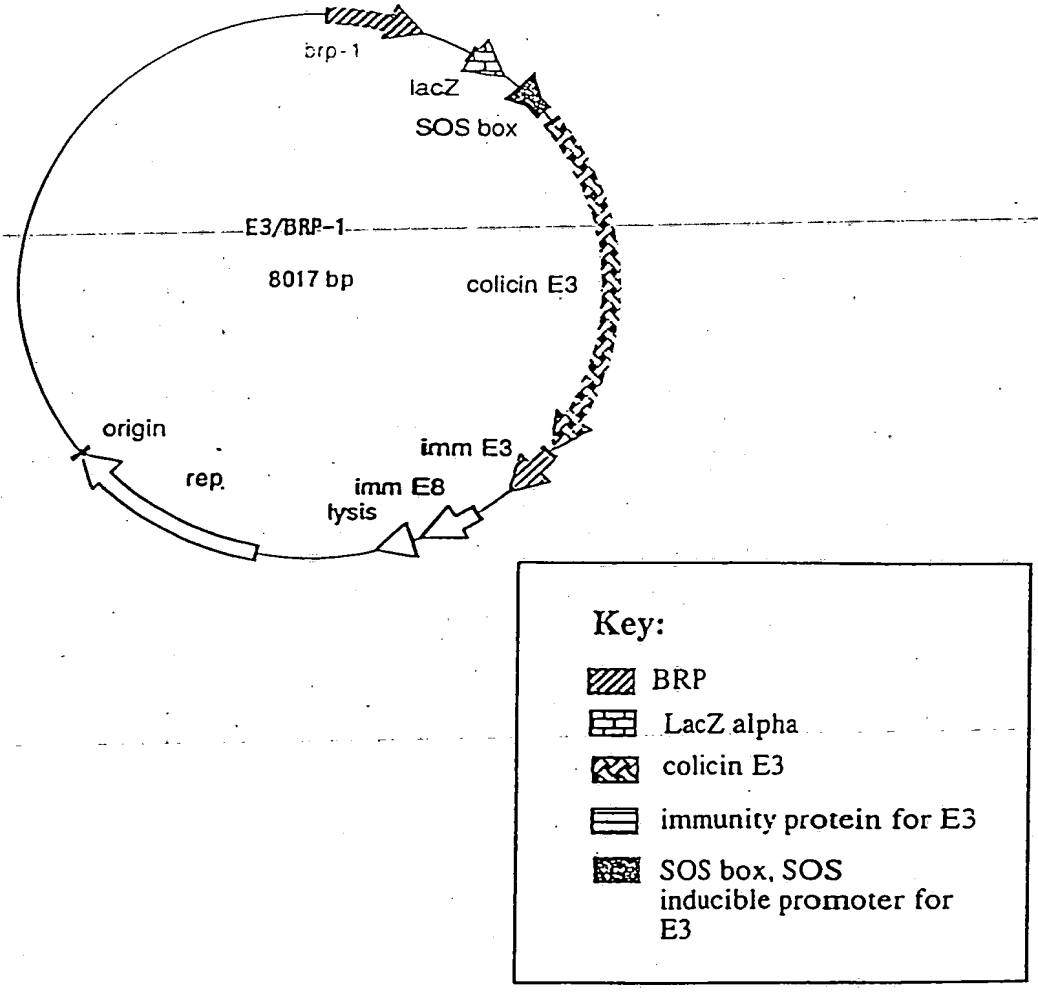

brp-1
lacZ
SOS box
E3/BRP-1
8017 bp
colicin E3
origin
rep
imm E3
imm E8
lysis
Key:
BRP
LacZ alpha
colicin E3
immunity protein for E3
SOS box, SOS inducible promoter for E3

FIG. 23

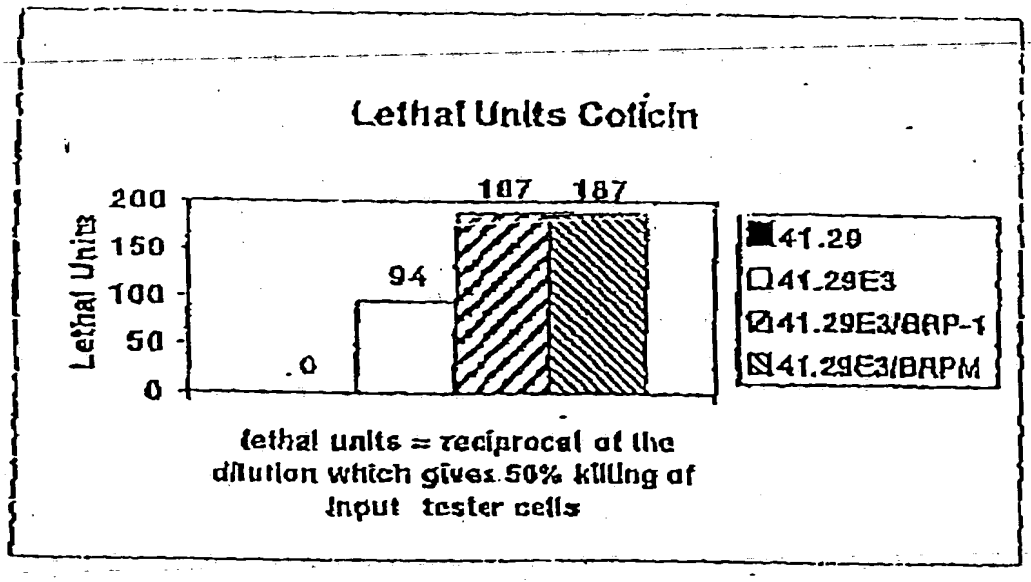

Lethal Units Colicin
Lethal Units
200
150
100
50
0
.0
94
187
187
41.29
41.29E3
41.29E3/BRP-1
41.29E3/BRPM
lethal units = reciprocal of the dilution which gives 50% killing of input tester cells

FIG. 24

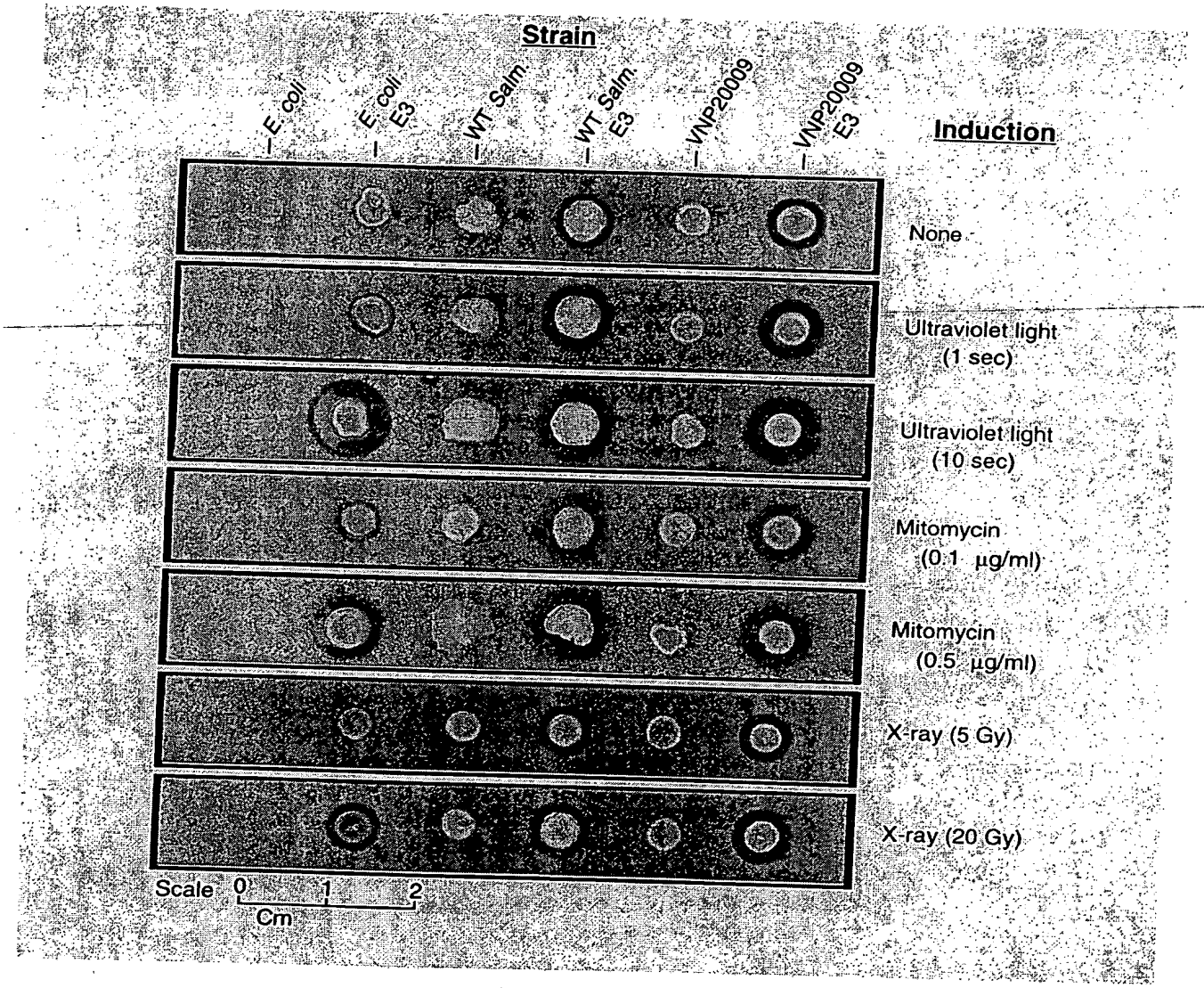

Strain
E. coli
E. coli E3
WT Salm.
WT Salm. E3
VNP20009
VNP20009 E3
Induction
None
Ultraviolet light (1 sec)
Ultraviolet light (10 sec)
Mitomycin (0.1 µg/ml)
Mitomycin (0.5 µg/ml)
X-ray (5 Gy)
X-ray (20 Gy)
Scale 0 1 2
Cm

FIG. 25

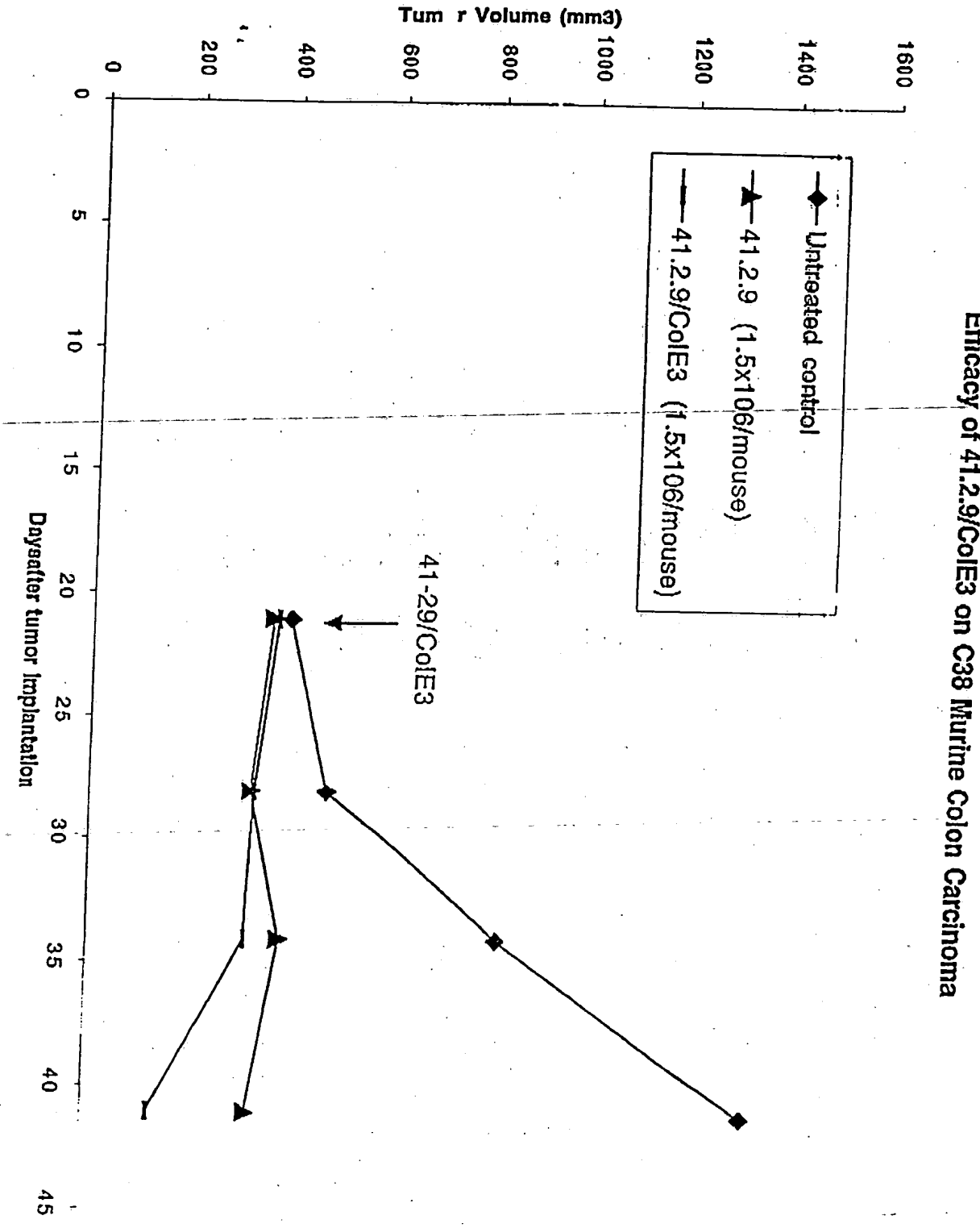

Efficacy of 41.2.9/ColE3 on C38 Murine Colon Carcinoma
Tumor Volume (mm3)
0
200
400
600
800
1000
1200
1400
1600
0
5
10
15
20
25
30
35
40
45
Dayafter tumor implantation
Untreated control
41.2.9 (1.5x106/mouse)
41.2.9/ColE3 (1.5x106/mouse)
41-29/ColE3

FIG. 26

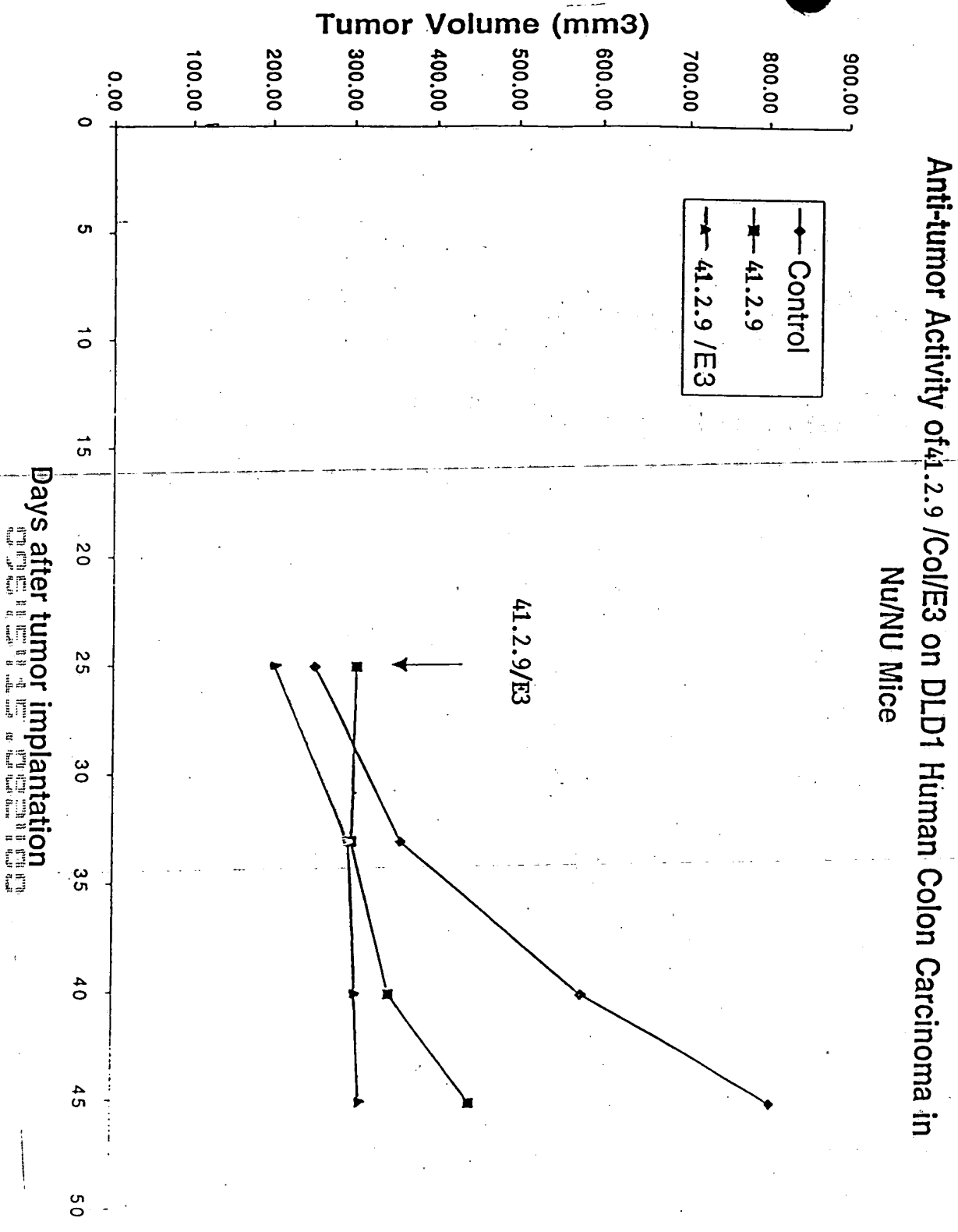

Anti-tumor Activity of41.2.9 /Col/E3 on DLD1 Human Colon Carcinoma in Nu/NU Mice
Tumor Volume (mm3)
0.00
100.00
200.00
300.00
400.00
500.00
600.00
700.00
800.00
900.00
0
5
10
15
20
25
30
35
40
45
50
Days after tumor implantation
Control
41.2.9
41.2.9 /E3
41.2.9/E3

FIG. 27

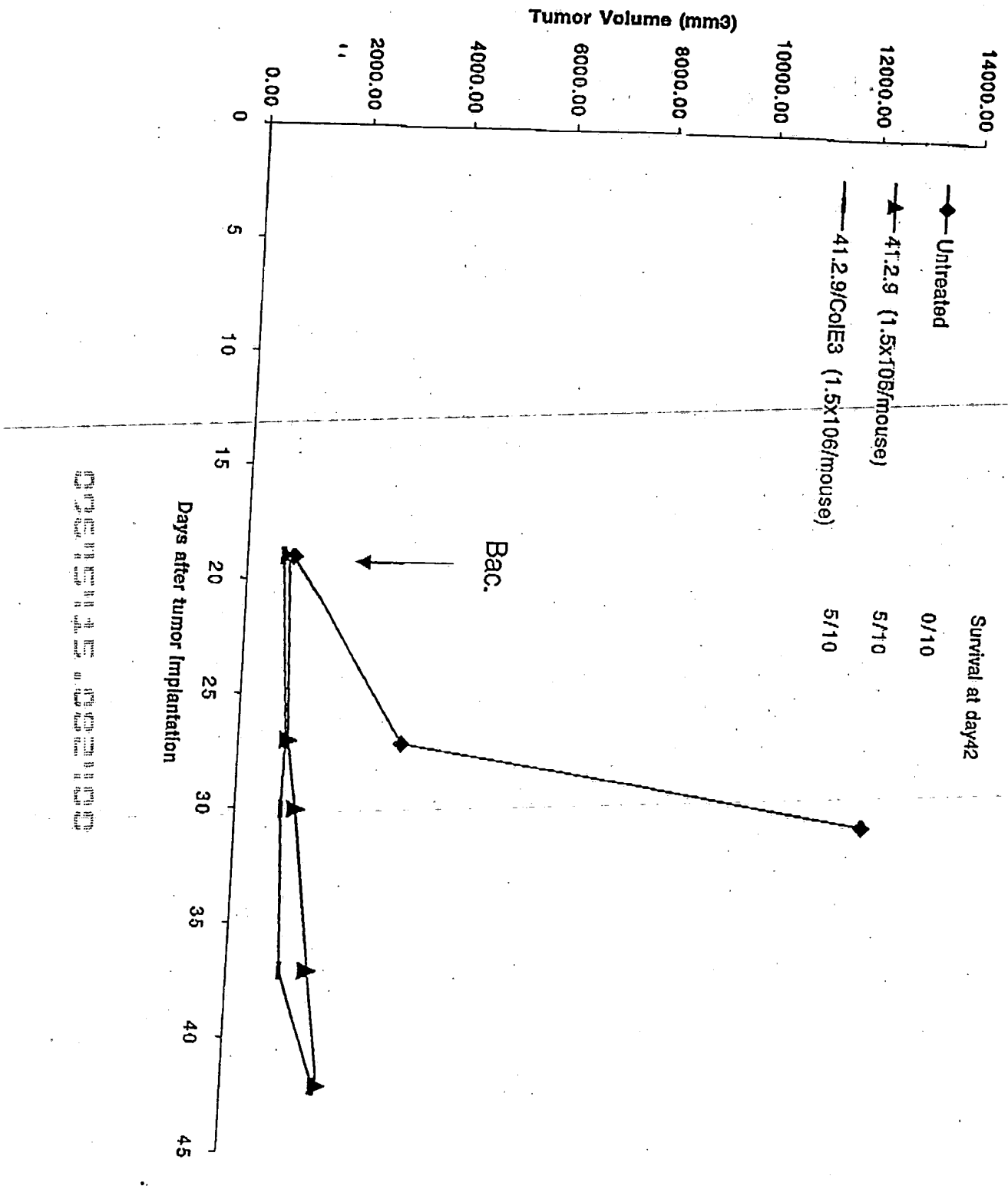

Efficacy of 41.2.9/ColE3 on B16 Murine Melanoma
Tumor Volume (mm3)
0.00
2000.00
4000.00
6000.00
8000.00
10000.00
12000.00
14000.00
0
5
10
15
20
25
30
35
40
45
Days after tumor implantation
Bac.
Untreated
41.2.9 (1.5x106/mouse)
41.2.9/ColE3 (1.5x106/mouse)
Survival at day42
0/10
5/10
5/10

FIG. 28

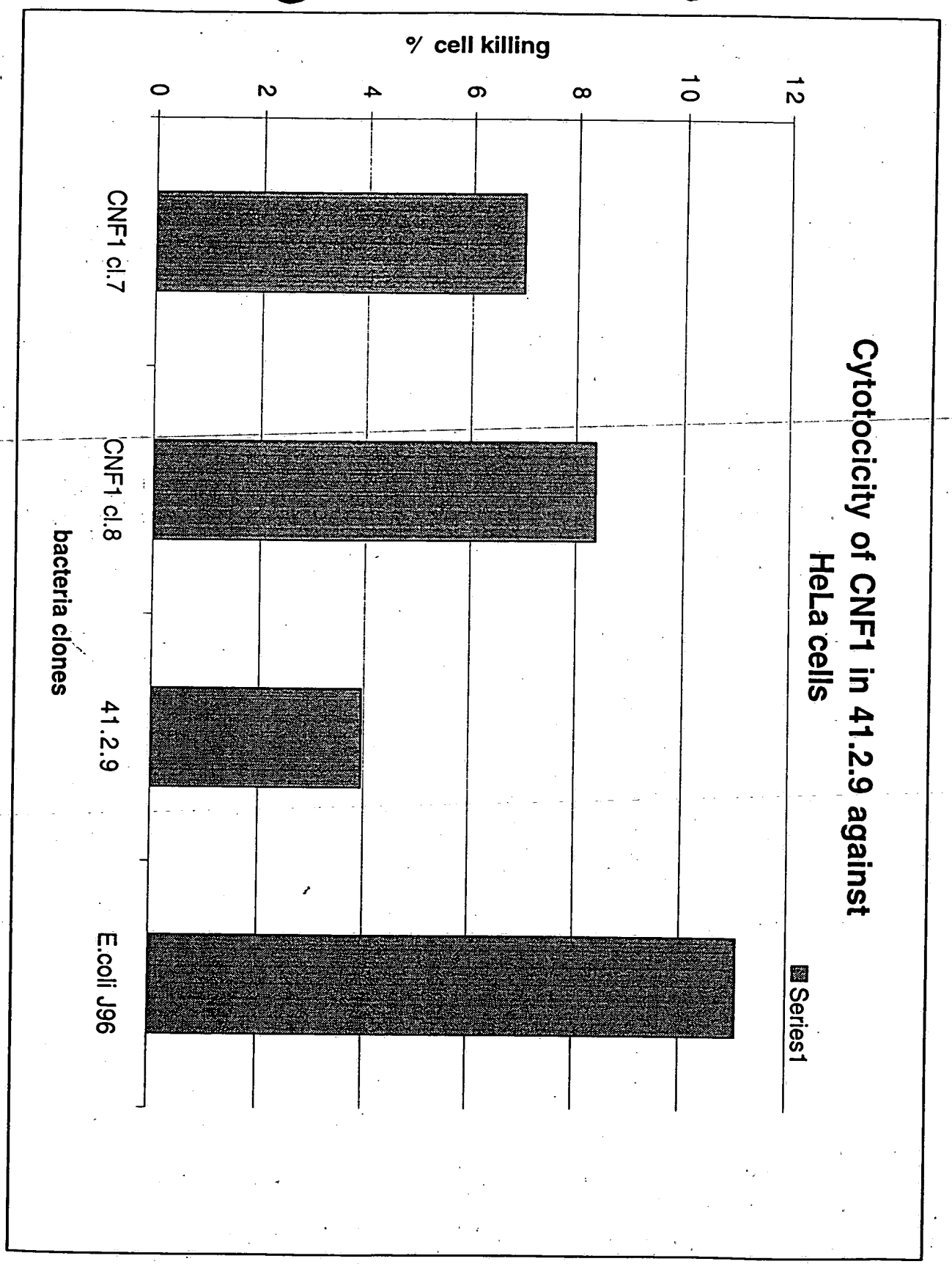
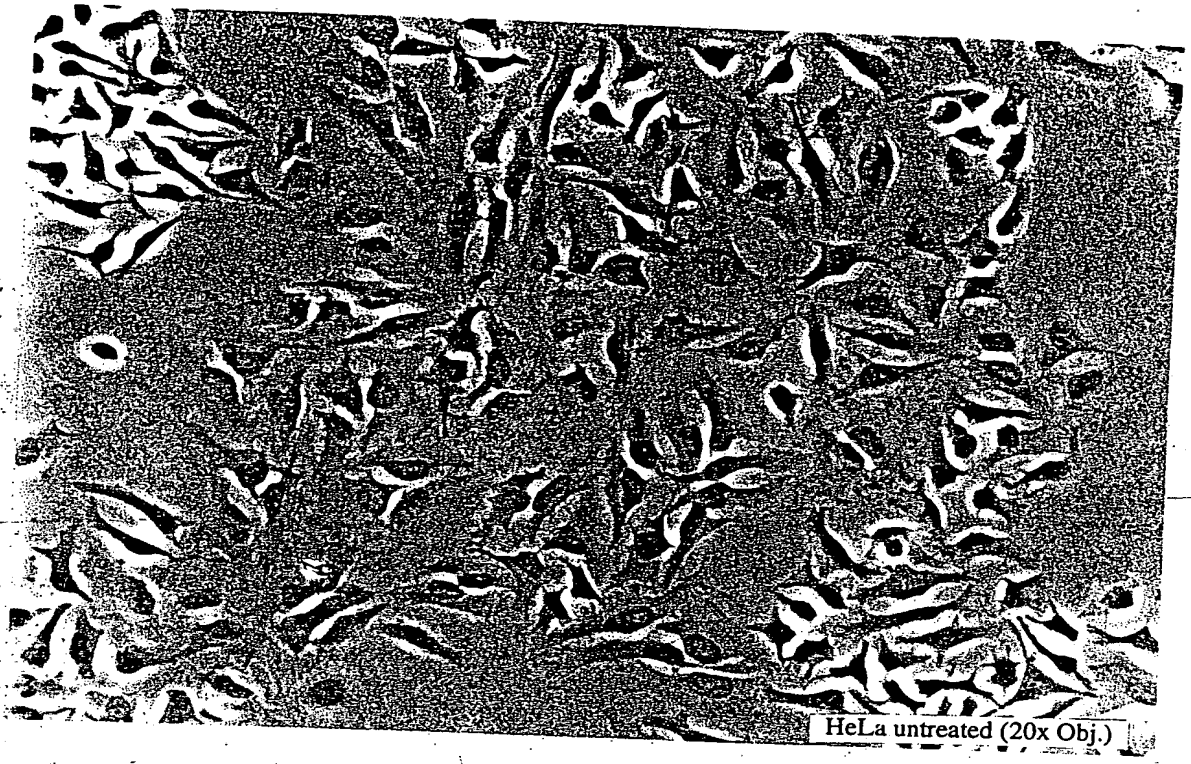

Cytotocicity of CNF1 in 41.2.9 against HeLa cells
% cell killing
0
2
4
6
8
10
12
CNF1 cl.7
CNF1 cl.8
41.2.9
E.coli J96
bacteria clones
Series1

FIG. 29

A



B

FIG. 30

```
GATATCATTC TGGCCTCTGA CGTTGTGATG GTCGCACGTG GCGATCTGGG CGTTGAAATC GGCGATCCGG      70
AGCTGGTTGG TATCCAGAAA GCGCTGATTC GCCGTGCGCG TCAGCTAAAC CGCGCAGTCA TCACCGCAAC     140
GCAAATGATG GAGTCGATGA TCACCAACCC GATGCCGACC CGTGCGGAAG TGATGGACGT GGCGAACGCC     210
GTCCTGGATG GCACGGATGC GGTTATGCTG TCTGCCGAAA CCGCAGCCGG TCAGTATCCT TCTGAAACCG     280
TTGCCGCAAT GGCGCGCGTC TGCCTGGGCG CAGAAAAAAT CCCCAGCATC AATGTGTCTA AACACCGTCT     350
CGACGTGCAG TTCGACAACG TTGAAGAAGC CATTGCCATG TCTGCGATGT ATGCGGCAAA CCATCTGAAA     420
GGCGTTACCG CGATCATCAC CATGACGGAA TCCGGTCGTA CCGCGCTAAT GACTTCCCGT ATCAGCTCCG     490
GCCTGCCGAT TTTCGCCATG TCGCGCCATG AACGCACGCT GAACCTGACC GCGCTCTATC GCGGAGTAAC     560
GCCGGTGCAT TTTGATAGCG CGGCTGATGG CGTTGTCGCG GCACATGAAG CTGTTAATCT GCTGCGCGAT     630
AAAGGGTATC TGGTTTCCGG CGACCTGGTT ATCGTGACCC AGGGCGATGT CATGAGCACC GTCGGTTCAA     700
CCAATACCAC GCGGCCGCCC CCTTAATTAA CCCCGCATGC GGGGGGCCAT ATAGGCCGGG GATTTAAATG     770
CAAACGTCCG CCGAAACGCC GACGCACTGT GTTCCAGATA TAGTCAAAAA CCGGATTACC CTGATTATGA     840
AACATCGCCG CCATTTTTTG CCCCTGAGAG GCCATCAGCA TGGCTGGAAT GTCGACGCCC CAGCCATGCG     910
GTACGAGAAA AATGACTTTT TCGTCGTTAC GACGCATCTC CTCGATAATC TCCAGACCTT CCCAGTCAAC     980
ACGCTGTTGA ATTTTTTTCG GACCGCGCAT CGCCAACTCA GCCATCATCG CCATTGCCTG TGGCGCGGTG    1050
GCGAACATCT CATCGACAAT CGCTTCGCGC TCAGCTTCGC TACGCTGCGG AAAGCACAAC GACAGATTAA    1120
TTAGCGCCCG GCGACGAGAA CTCTTCCCCA GCCGTCCGGC AAAACGCCCC AGCGTCGCCA GCAAAGGGTC    1190
GCGGAATGAT GCCGGTGTTA ATGCGATCCC CGCCATTGCC GCCGCGCCCA ACCAGGCGCC CCAATACTGT    1260
GGATAGCGAA AGGATTTTTC GAATTCAGGG ATATACTCAC TATTATTTTT TTTGGTTTCC ATGCTTTTCC    1330
AGGGTCTGCT GACGCGAAAA GGAATTGTGA ATAGTGTAGC GACGTCTGCG TCTCACACAA AACAAAAAAG    1400
CCGGCACACA TCGCGTACCG GCTCTGTCAG CGCATTTGTT AATCGAAGCG CAGTTGCGGC AGAACCTCTT    1470
TCACCTGTGC CAGGTATTCA CGACGATCTG ACCCCGTCAG ACCTTCCGTG CGCGGCAATT TTGCTGTCAG    1530
AGGGTTAACG GCTTGCTGGT TGATC                                                     1555
```

FIG. 31

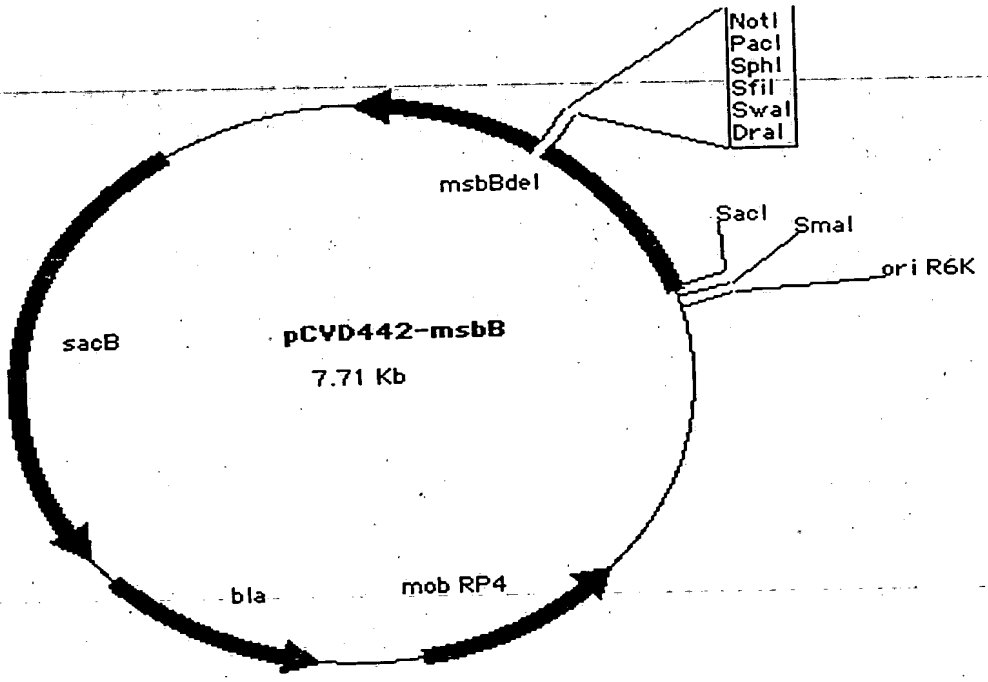

NotI
PacI
SphI
SfiI
SwaI
DraI
msbBdel
SacI
SmaI
ori R6K
sacB
pCVD442-msbB
7.71 Kb
bla
mob RP4

FIG. 32

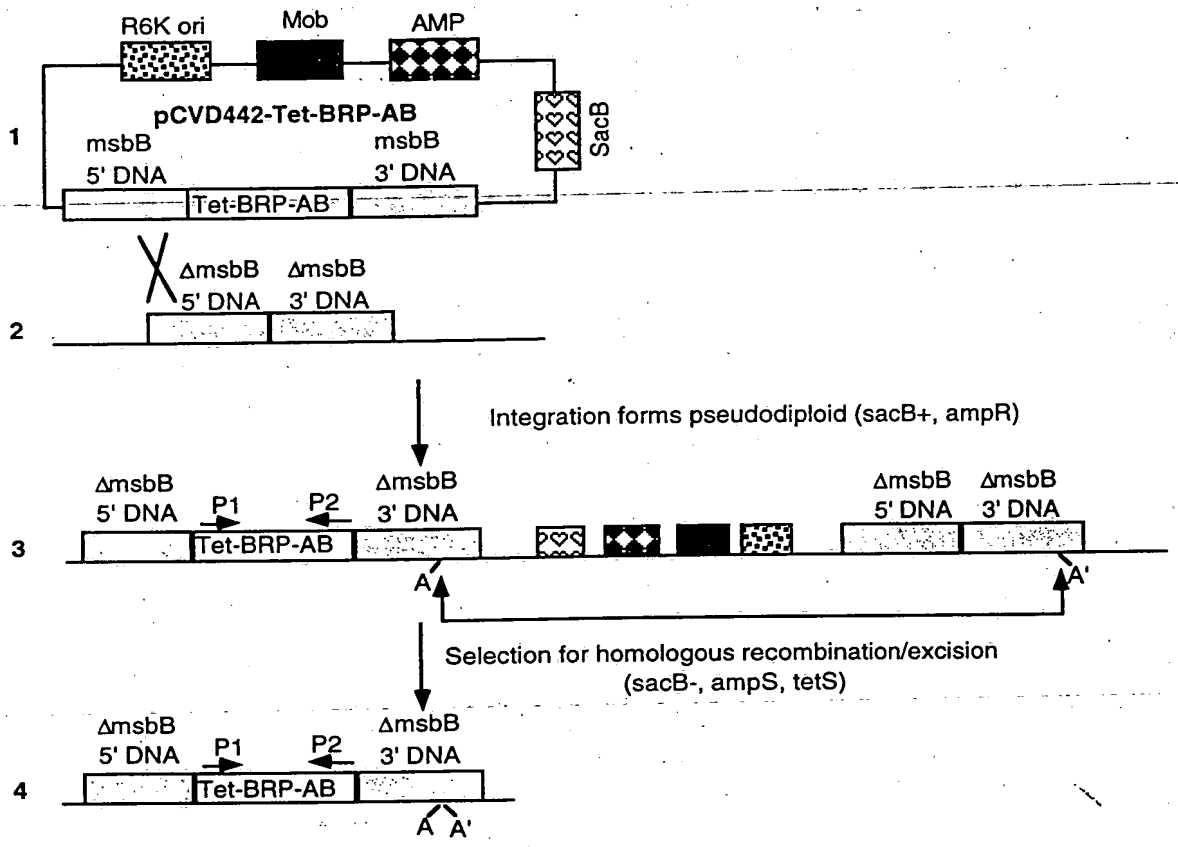

R6K ori
Mob
AMP
pCVD442-Tet-BRP-AB
msbB
5' DNA
msbB
3' DNA
Tet-BRP-AB
SacB
1
ΔmsbB
5' DNA
ΔmsbB
3' DNA
2
Integration forms pseudodiploid (sacB+, ampR)
ΔmsbB
5' DNA
P1
P2
ΔmsbB
3' DNA
Tet-BRP-AB
ΔmsbB
5' DNA
ΔmsbB
3' DNA
3
A
A'
Selection for homologous recombination/excision
(sacB-, ampS, tetS)
ΔmsbB
5' DNA
P1
P2
ΔmsbB
3' DNA
Tet-BRP-AB
4
A
A'

FIG.33

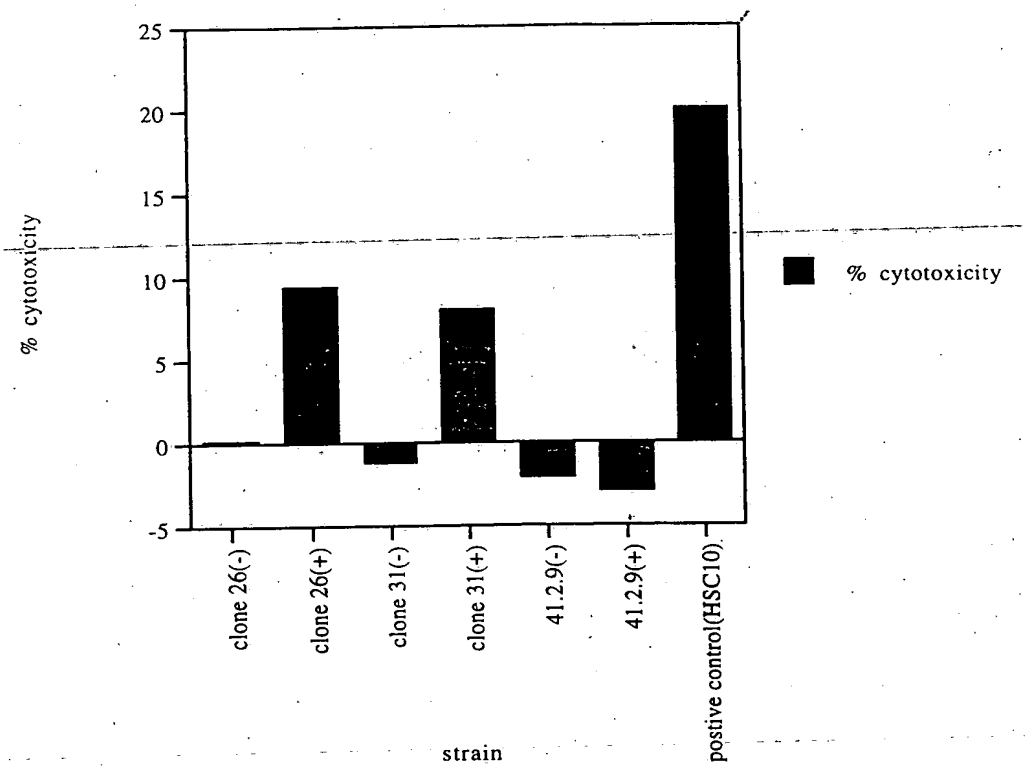

25
20
15
10
5
0
-5
% cytotoxicity
clone 26(-)
clone 26(+)
clone 31(-)
clone 31(+)
41.2.9(-)
41.2.9(+)
postive control(HSC10)
strain
% cytotoxicity

FIG. 34

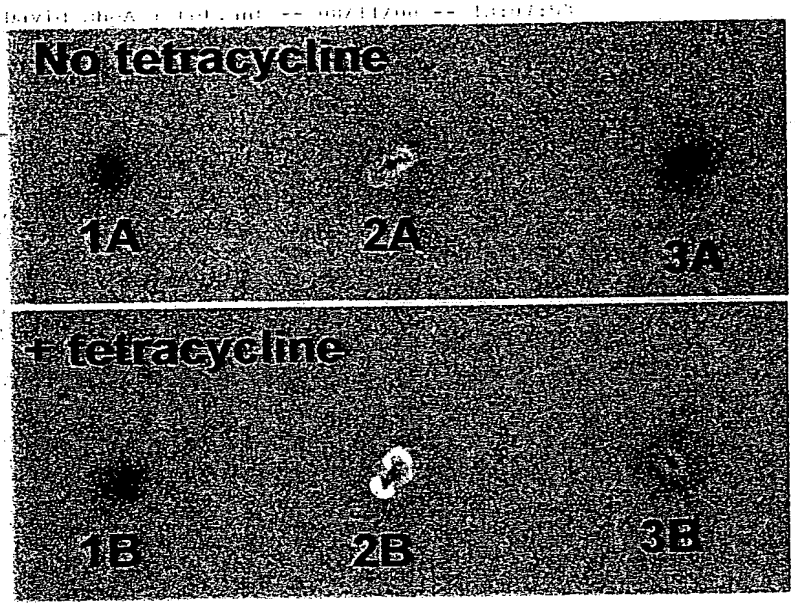


FIG. 35

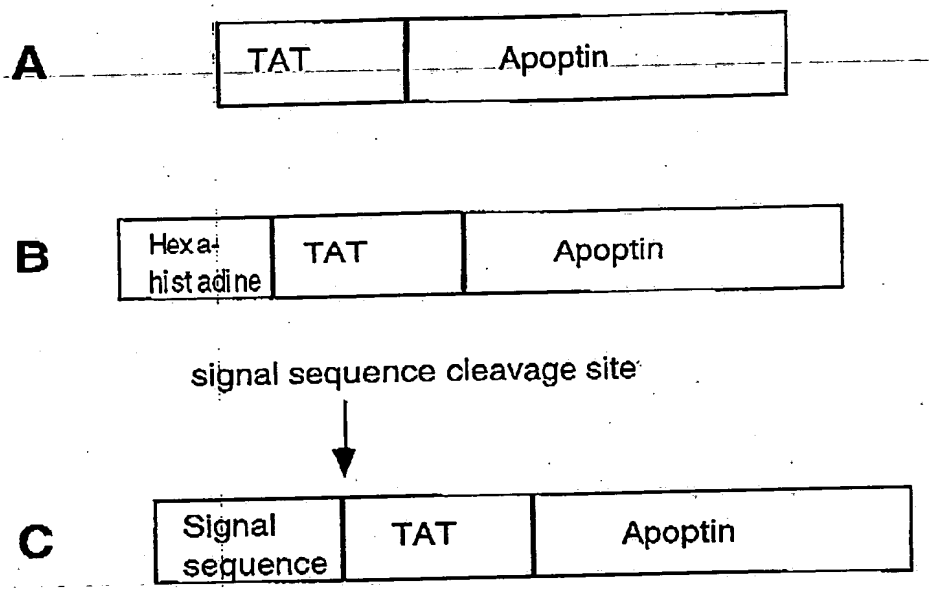

A
TAT
Apoptin
B
Hexa-histadine
TAT
Apoptin
signal sequence cleavage site
C
Signal sequence
TAT
Apoptin

FIG. 36

Protein Sequence of 616-4 F

Length of 616-4 F: 551 bp; Listed from: 1 to: 551;
Translated from: 7 to: 409 (Entire region);
Genetic Code used: Universal; Wed, Aug 16, 2000 1:40 PM

Frame 1

```
          M   A   Y   G   R   K   K   R   R   Q   R   R   R   M   N
NAG ACC ATG GCT TAT GGC AGA AAA AAA AGA AGA CAG AGA AGA AGA ATG AAC
              9          18          27          36          45

A   L   Q   E   D   T   P   P   G   P   S   T   V   F   R   P   P   T   S
GCG CTG CAG GAA GAT ACC CCG CCG GGC CCG TCC ACC GTG TTT CGC CCG CCG ACC TCC
      60          69          78          87          96          105

S   R   P   L   E   T   P   H   C   R   E   I   R   I   G   I   A   G   I
TCC CGC CCG CTG GAA ACC CCG CAT TGC CGC GAA ATC CGC ATC GGC ATC GCG GGC ATC
      117         126         135         144         153         162

T   I   T   L   S   L   C   G   C   A   N   A   R   A   P   T   L   R   S
ACC ATC ACC CTG TCC CTG TGC GGC TGC GCG AAC GCG CGC GCG CCG ACC CTG CGC TCC
      174         183         192         201         210         219

A   T   A   D   N   S   E   N   T   G   F   K   N   V   P   D   L   R   T
GCG ACC GCG GAT AAC TCC GAA AAC ACC GGC TTT AAA AAC GTC CCG GAT CTG CGC ACC
      231         240         249         258         267         276

D   Q   P   K   P   P   S   K   K   R   S   C   D   P   S   E   Y   R   V
GAT CAG CCG AAA CCG CCG TCC AAA AAA CGC TCC TGC GAT CCG TCC GAA TAT CGC GTC
      288         297         306         315         324         333

S   E   L   K   E   S   L   I   T   T   T   P   S   R   P   R   T   A   R
TCC GAA CTG AAA GAA TCC CTG ATC ACC ACC ACC CCG TCC CGC CCG CGC ACC GCC CGC
      345         354         363         372         381         390

R   C   I   R   L   .
CGC TGC ATC CGC CTC TGA AAG CTT GGC TGT TTT GGC GGA TGA GAG AAG ATT TTC AGC
      402         411         420         429         438         447

CTG ATA CAG ATT AAA TCA GAA CGC AGA AGC GGT CTG ATA AAA CAG AAT TTG CCT GGC
      459         468         477         486         495         504

GGC AGT AGC GCG GTG GTC CCA CCT GAC CCC ATG CCG AAC TCA GA
      516         525         534         543
```

FIG. 37

Protein Sequence of TAP6H8 trcF

Length of TAP6H8 trcF: 751 bp; Listed from: 1 to: 444;
Translated from: 7 to: 427 (Entire region);
Genetic Code used: Universal; Mon, Aug 14, 2000 3:19 PM

Frame 1

```
          M   A   H   H   H   H   H   H   Y   G   R   K   K   R   R
NAG ACC ATG GCT CAT CAC CAT CAC CAC CAT TAT GGC CGC AAA AAA CGC CGT
              9          18          27          36          45

Q   R   R   R   M   N   A   L   Q   E   D   T   P   P   G   P   S   T   V
CAG CGC CGT CGC ATG AAC GCG CTG CAG GAA GAT ACC CCG CCG GGC CCG TCC ACC GTG
        60          69          78          87          96         105

F   R   P   P   T   S   S   R   P   L   E   T   P   H   C   R   E   I   R
TTT CGC CCG CCG ACC TCC TCC CGC CCG CTG GAA ACC CCG CAT TGC CGC GAA ATC CGC
        117         126         135         144         153         162

I   G   I   A   G   I   T   I   T   L   S   L   C   G   C   A   N   A   R
ATC GGC ATC GCG GGC ATC ACC ATC ACC CTG TCC CTG TGC GGC TGC GCG AAC GCG CGC
        174         183         192         201         210         219

A   P   T   L   R   S   A   T   A   D   N   S   E   N   T   G   F   K   N
GCG CCG ACC CTG CGC TCC GCG ACC GCG GAT AAC TCC GAA AAC ACC GGC TTT AAA AAC
        231         240         249         258         267         276

V   P   D   L   R   T   D   Q   P   K   P   P   S   K   K   R   S   C   D
GTC CCG GAT CTG CGC ACC GAT CAG CCG AAA CCG CCG TCC AAA AAA CGC TCC TGC GAT
        288         297         306         315         324         333

P   S   E   Y   R   V   S   E   L   K   E   S   L   I   T   T   T   P   S
CCG TCC GAA TAT CGC GTC TCC GAA CTG AAA GAA TCC CTG ATC ACC ACC ACC CCG TCC
        345         354         363         372         381         390

R   P   R   T   A   R   R   C   I   R   L   .
CGC CCG CGC ACC GCC CGC CGC TGC ATC CGC CTC TGA AAG CTT GGC TGT TTT
        402         411         420         429         438
```

FIG. 38

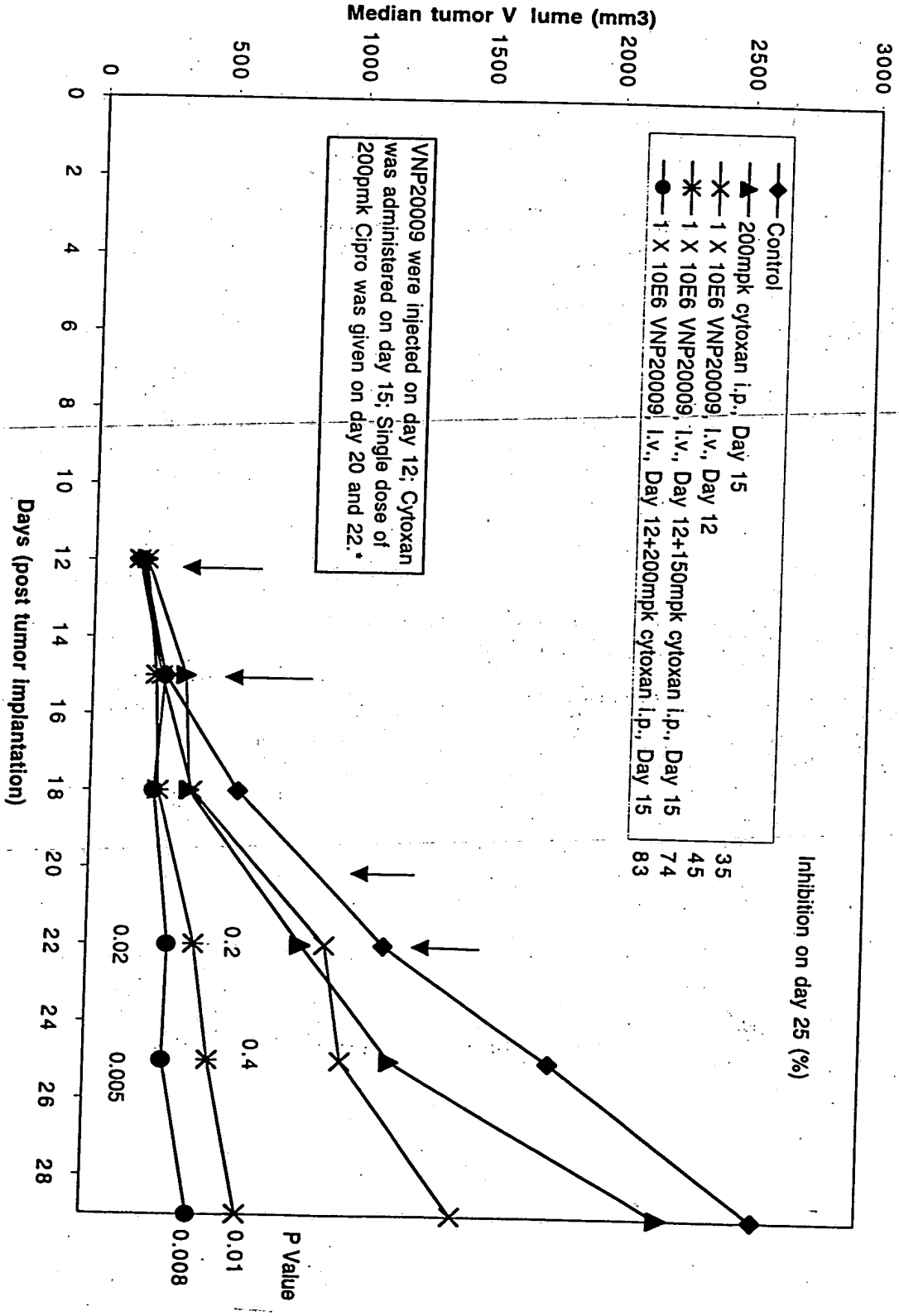

Median tumor V lume (mm3)
0
500
1000
1500
2000
2500
3000
Days (post tumor implantation)
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Control
200mpk cytoxan i.p., Day 15
1 X 10E6 VNP20009, i.v., Day 12
1 X 10E6 VNP20009, i.v., Day 12+150mpk cytoxan i.p., Day 15
1 X 10E6 VNP20009, i.v., Day 12+200mpk cytoxan i.p., Day 15
VNP20009 were injected on day 12; Cytoxan was administered on day 15; Single dose of 200pmk Cipro was given on day 20 and 22.*
Inhibition on day 25 (%)
35
45
74
83
P Value
0.02
0.2
0.005
0.4
0.008
0.01

FIG. 39

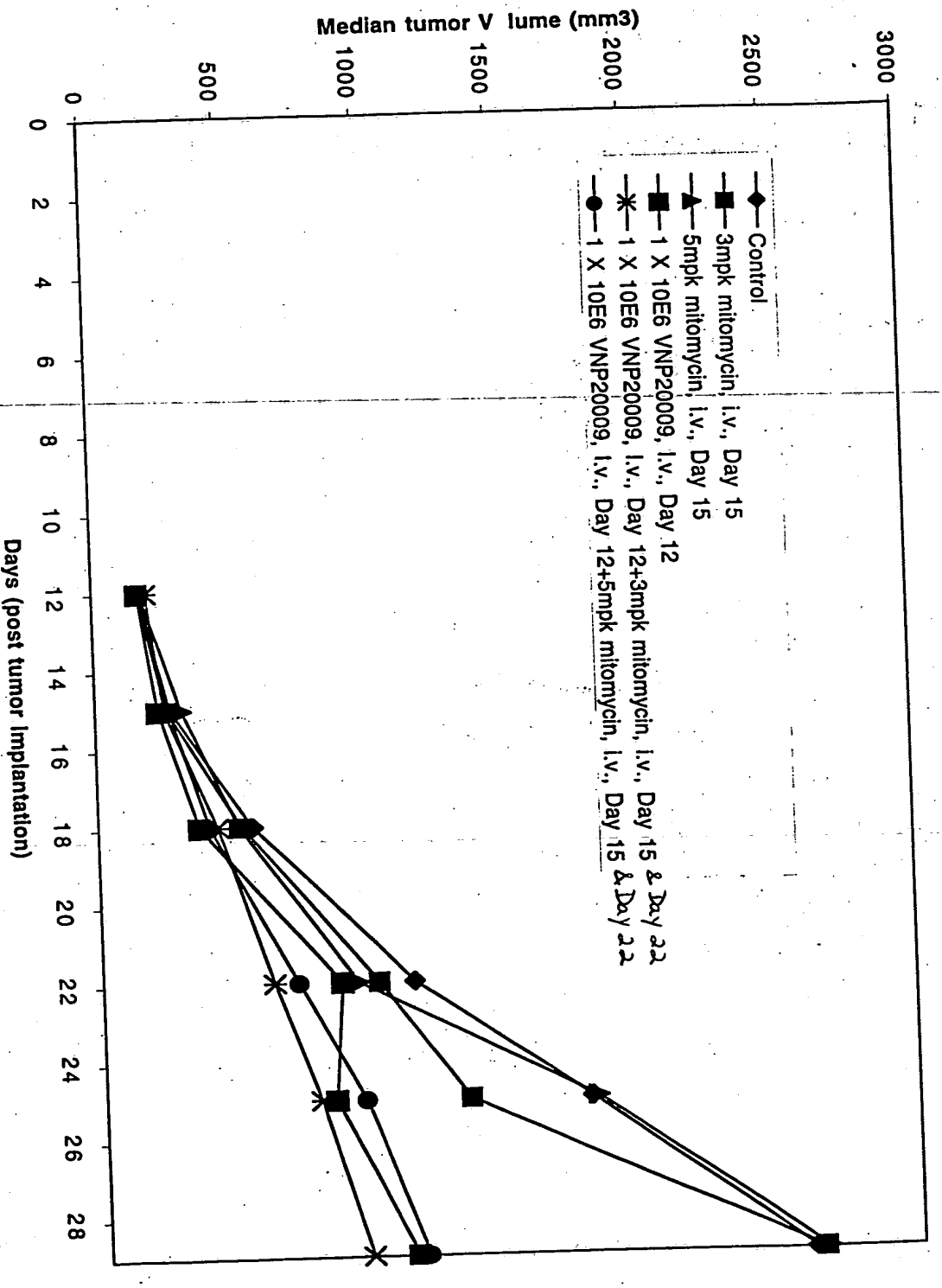

Median tumor V lume (mm3)
0
500
1000
1500
2000
2500
3000
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Days (post tumor Implantation)
Control
3mpk mitomycin, i.v., Day 15
5mpk mitomycin, i.v., Day 15
1 X 10E6 VNP20009, i.v., Day 12
1 X 10E6 VNP20009, i.v., Day 12+3mpk mitomycin, i.v., Day 15 & Day 22
1 X 10E6 VNP20009, i.v., Day 12+5mpk mitomycin, i.v., Day 15 & Day 22

FIG. 40

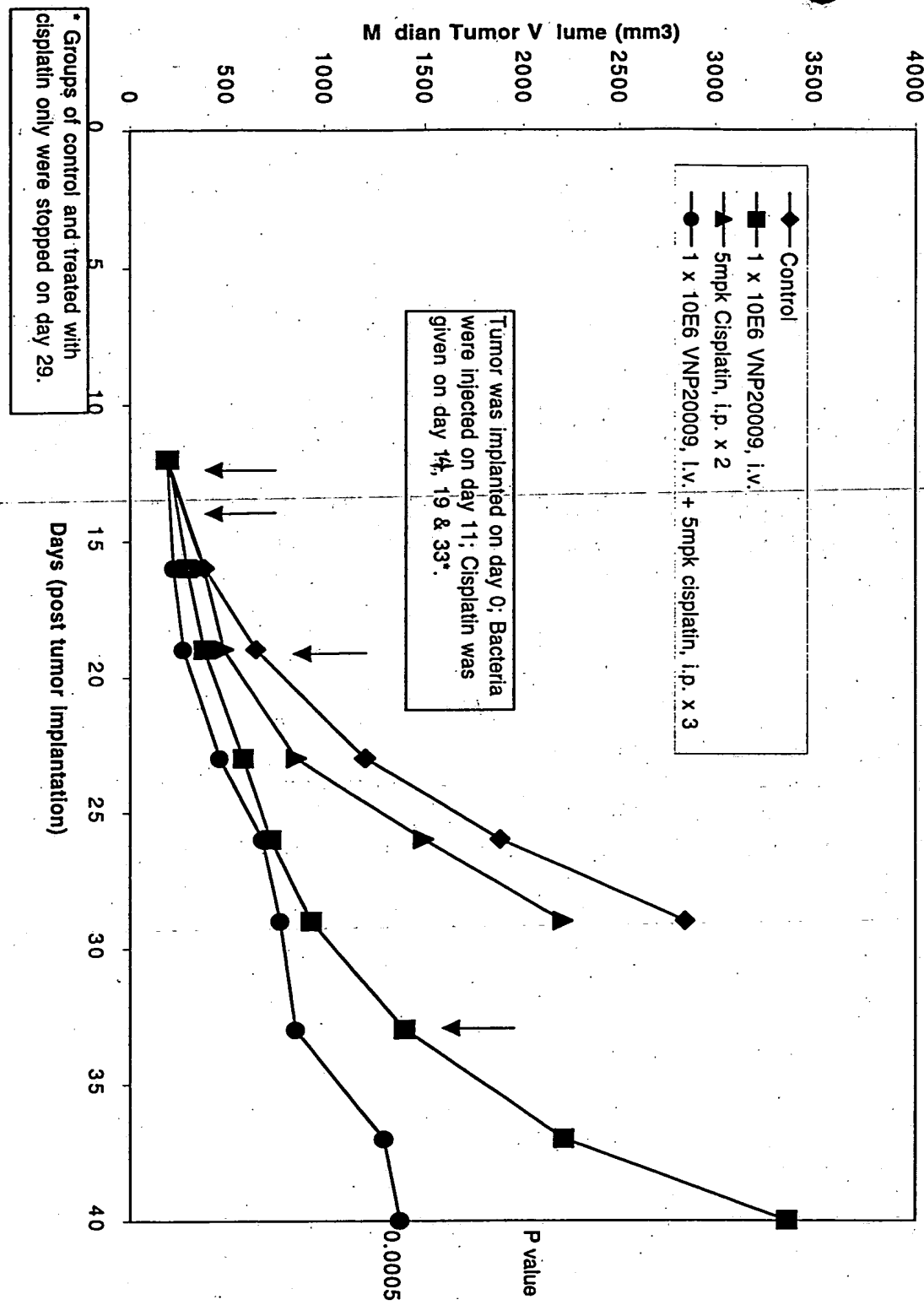

Median Tumor Volume (mm3)
0
500
1000
1500
2000
2500
3000
3500
4000
0
5
10
15
20
25
30
35
40
Days (post tumor implantation)
Control
1 x 10E6 VNP20009, i.v.
5mpk Cisplatin, i.p. x 2
1 x 10E6 VNP20009, i.v. + 5mpk cisplatin, i.p. x 3
Tumor was implanted on day 0; Bacteria were injected on day 11; Cisplatin was given on day 14, 19 & 33*.
* Groups of control and treated with cisplatin only were stopped on day 29.
P value
0.0005

FIG. 41